

# Clinical Trials in Multiple Sclerosis 2009: Planned, In Progress, Recently Completed

This listing is prepared on behalf of the National Multiple Sclerosis Society's Advisory Committee on Trials of New Drugs in MS from materials provided by principal investigators and from information gathered from published literature and public presentations. While we strive for accuracy and completeness, there are surely additional trials that are not included. Because clinical trials are dynamic studies, there may be inaccuracies due to changes in protocol for selected studies.

**Trial Information:** Where information was not provided to us or has not been reported, we have indicated that this information is "Not available." Trials that have been completed or terminated are marked as such. These studies will be removed after two years. We maintain an archive of older lists, in case of an inquiry, and published studies can be found on PubMed <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>.

**ClinicalTrials.gov:** Where available, we have provided the link to the study listing on the ClinicalTrials.gov Web site (<http://www.clinicaltrials.gov/>). A statement from the International Committee of Medical Journal Editors released in September 2004 required investigators to register clinical trials, except studies designed to study pharmacokinetics or major toxicity, such as phase 1 trials (*The New England Journal of Medicine* 2004 Sep 16;351(12):1250-1). For studies not registered at the time this list was compiled, this information is cited as "Not available."

## **Clinical Trials Participation: Resources Available on our Web Site**

- A database of trials recruiting people with MS that is searchable by state, type of MS, and keyword, and includes a list of international studies.
- "MS Trial Alerts" highlighting specific studies.
- Materials designed to help people understand clinical trial participation, including a brochure, an online course, and FAQs.

<http://www.nationalmssociety.org/clinicaltrials>



National  
Multiple Sclerosis  
Society

JOIN THE MOVEMENT  
[www.nationalmssociety.org](http://www.nationalmssociety.org)

Research & Clinical Programs  
National Multiple Sclerosis Society  
733 Third Avenue, New York, NY 10017  
Tel: (212) 476-0411; Fax: (212) 986-7981

## Index of Agents

<b>Agent (Generic name or description)</b>	<b>Hyperlinks to Pages</b>
3-4 diaminopyridine .....	6
Albuterol (Proventil®, Schering Corporation) .....	33
Alemtuzumab (Genzyme Corporation) .....	6-7
Aspirin .....	8
Atacicept.....	8
ATL1102 .....	9
Atorvastatin (Lipitor®, Pfizer Ireland Pharmaceuticals Corp.) .....	9-10,14
ATX-MS1467 .....	10
AVP-923 (Zenvia™, Avanir Pharmaceuticals).....	11
BAF312.....	12
BG00012 (dimethyl fumarate).....	12-13
BHT-3009 .....	14
Bone marrow/peripheral stem cell transplantation (autologous) .....	15-16
Botulinum toxin A (Botox®, Allergan, Inc.) .....	16-17
C-105 (l amphetamine sulfate) .....	18
Cannabis extract (cannador).....	18
Cannabis extract (dronabinol vs. cannabis).....	19
Cannabis extract (dronabinol) .....	19
Cannabis extract (tetrahydrocannabinol and cannabidiol, Sativex®, GW Pharmaceuticals).....	20
CDP323 .....	21
Chaperonin 10 .....	21
Cladribine .....	22
CNTO 1275 (monoclonal antibody).....	23
Cyclophosphamide.....	23-24
Daclizumab .....	24-25
Donepezil (Aricept®, Eisai Co.).....	25
Doxycycline + interferon beta-1a (Avonex®, Biogen Idec) .....	26
Duloxetine hydrochloride (Cymbalta®, Lilly) .....	26
Estradiol .....	58
Estriol.....	27
Estroprogestins.....	39
Fampridine-SR (4-aminopyridine, sustained release).....	27
Fingolimod (FTY720) .....	28-30
Fish oil .....	30
Ginkgo biloba .....	31
Ginseng.....	31
Glatiramer acetate (Copaxone®, Teva Pharmaceutical Industries Ltd.) .....	13,32-34,36, 40-41,50
Helminth-induced immunomodulation therapy.....	35
Interferon beta-1a (Avonex®, Biogen Idec) .....	26,30,35-37,44, 47,50,51,52,65

Interferon beta-1a (Rebif®, EMD Serono and Pfizer Inc.) .....	6,7,10,22, 38-40
Interferon beta-1b (Betaseron®, Bayer HealthCare Pharmaceuticals, Inc.) .....	40-41,50
Interferon tau.....	42
Lamotrigine (Lamictal®, GlaxoSmith Kline).....	42
Laquinimod.....	43-44
MBP8298 (dirucotide) .....	44-45
Memantine (Namenda®, Forest Pharmaceuticals) .....	46
Methotrexate.....	36
Methylprednisolone .....	24,36-37,46
Minocycline.....	47
Mitoxantrone for injection concentrate (Novantrone®, EMD Serono) .....	33-34,37,48-50
MN-166 .....	51
Mycophenolate mofetil (CellCept®, Roche Laboratories, Inc.) .....	51-52
Low dose naltrexone.....	52
Natalizumab (Tysabri®, Biogen Idec and Elan) .....	53-54
Nerispiridine .....	55
Ocrelizumab.....	55
PI-2301 (co-polymer) .....	56
Pixantrone (BBR 2778) .....	56
Plasmapheresis (plasma exchange) .....	57
Pravastatin (Pravachol®, Bristol-Myers Squibb).....	57
Prednisone.....	36
Pregabalin (Lyrica®, Pfizer, Inc.) .....	58
aroxetine (Paxil®, GlaxoSmith Kline) .....	58
Progesterone .....	58
Rehabilitation.....	59-60
Repetitive Transcranial Magnetic Stimulation (rTMS) .....	61
RG2077.....	61
Riluzole (Rilutek®, Sanofi-aventis) .....	62
Rituximab (Rituxan®, Genentech and Biogen Idec).....	62-63
Rolipram (phosphodiesterase-4 inhibitor).....	64
RTL1000.....	64
SB-683699 .....	65
Simvastatin .....	65
Stress management program .....	66
T cell vaccination (Tovaxin™, Opexa Therapeutics).....	66
T cell receptor peptide vaccine (NeuroVax™, Orchestra Therapeutics) .....	67
Teriflunomide (HMR1726).....	57-69
vitamin D3 .....	69

## Index by type of MS/type of patient

Relapsing-remitting.....	7-9,12-15,18,20-23,25-45,47-52,54-57,60-69
Secondary-progressive.....	8,10,14,18-19,21,24,42,45,48-51,56,60,64,66,69
Primary-progressive .....	19,29,49,52,60,63
Progressive-relapsing .....	15,20,33,69
All types .....	6,16-18,25-27,30-31,35,46,55,58-59,69
At risk (CIS, first clinical demyelinating event suggestive of MS) .....	9,10,32,40,47,62,66,68
Relapsing forms.....	22,38,53-54,58
With specific symptoms .....	11,18,20,26,55,58
Women .....	27,39,58

## **Abbreviations Key**

**BBB** - blood brain barrier

**bid** - twice daily

**biw** - twice weekly

**EDSS** - Expanded Disability Status Scale

**G-CSF** - granulocyte colony-stimulating factor

**Gd** - gadolinium

**im** - intramuscular

**iv** - intravenous

**MSFC** - Multiple Sclerosis Functional Composite

**MSIS** - Multiple Sclerosis Impact Scale

**MSQLI** - Multiple Sclerosis Quality of Life Inventory

**MSQOL-54** - Multiple Sclerosis Quality of Life-54

**NRS** - Scripps Neurological Rating Scale

**PASAT** - Paced Auditory Serial Addition Test

**PBO** - placebo

**pc** - percutaneous

**po** - oral

**PP** - primary progressive

**PR** - progressive relapsing

**qhs** - at bedtime

**qhs** - every night

**qod** - every other day

**rATG** - rabbit antithymocyte globulin

**RR** - relapsing-remitting

**sc** - subcutaneous

**SF-36** - Short Form-36 derived from General Health Survey of Medical Outcomes Study

**SP** - secondary progressive

**tid** - three times daily

**tiw** - three times weekly

**Agent:** 3-4 diaminopyridine  
**Purpose of study:** To improve fatigue and quality of life  
**Possible mechanism:** Blocks potassium channels on axons, permitting demyelinated axon to transmit impulses  
**Study description:** Double blinded, placebo controlled, dose escalation  
**Dose/route:** 30-60 mg/d po vs. PBO po  
**Outcome parameters:** Fatigue Impact Scale, Visual Analogic Scale, quality of life  
**Type of MS:** All types  
**Number of Subjects:** 126  
**Start date:** February 2005  
**Observation period:** 8 weeks  
**Investigators:** P. Cesaro and others  
**Sites:** Hôpital Henri-Mondor-France, Creteil, and others, France  
**Results/Publications:** Not available  
**Funding:** French Health Ministry  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00190268>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif<sup>®</sup>, Serono Pfizer)

**COMPLETED**

**Purpose of study:** To control disease progression  
**Possible mechanism:** Targets CD52 antigen expressed on B and T lymphocytes (Campath)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)  
**Study description:** Open label  
**Dose/route:** Campath 12 mg/d iv for 5 days at mos 0, 12, 24 vs. Campath 24 mg/d iv for 5 days at mos 0, 12, 24 vs. Rebif 22 mcg tiw sc with dose increases over 4 wks to 44 mcg tiw sc for 36 mos  
**Outcome parameters:** Time to sustained accumulation of disability at 3 yrs  
**Type of MS:** RR  
**Number of Subjects:** 333  
**Start date:** November 2002  
**Observation period:** 36 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States and United Kingdom  
**Results/Publications:** Those taking alemtuzumab had a 74% reduction in the risk of MS relapse compared with those on Rebif, and a 71% reduction in the risk for sustained accumulation of disability; alemtuzumab group experienced adverse events more frequently, including immune thrombocytopenic purpura, thyroid adverse events, and infections (*New England Journal of Medicine* 2008 Oct 23;359(17):1786-801)  
**Funding:** Genzyme Corporation, Bayer Schering Pharma  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00050778>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif<sup>®</sup>, Serono Pfizer)  
**Purpose of study:** To compare effect on progression of disability and relapse rate, also known as CARE-MS I  
**Possible mechanism:** Targets CD52 antigen expressed on B and T lymphocytes (Campath)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)  
**Study description:** Examining MD blind  
**Dose/route:** Campath 12 mg/d iv for 5 days at mos 0, 12 vs. Rebif 22 mcg tiw sc  
**Outcome parameters:** Time to sustained accumulation of disability and relapse rate at 2 yrs  
**Type of MS:** RR  
**Number of Subjects:** 525  
**Start date:** September 2007  
**Observation period:** 2-4 years  
**Investigators:** Multiple  
**Sites:** Multicenter, North America, Europe, Latin America, Australia  
**Results/Publications:** Rationale and design described (Abstract #P02.171, AAN 2008)  
**Funding:** Genzyme Corporation, Bayer HealthCare Pharmaceuticals  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00530348>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Alemtuzumab (Genzyme Corporation) vs. interferon beta-1a (Rebif<sup>®</sup>, Serono Pfizer)  
**Purpose of study:** To test 2 doses of alemtuzumab versus interferon beta-1a on progression of disability and relapse rate, also known as CARE-MS II  
**Possible mechanism:** Targets CD52 antigen expressed on B and T lymphocytes (Campath)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)  
**Study description:** Examining MD blind  
**Dose/route:** Campath 12 mg/d iv for 5 days at mos 0, 12 vs. Campath 24 mg/d iv for 5 days at mos 0, 12 vs. Rebif 22 mcg tiw sc  
**Outcome parameters:** Time to sustained accumulation of disability and relapse rate at 2 yrs  
**Type of MS:** RR  
**Number of Subjects:** 1200  
**Start date:** October 2007  
**Observation period:** 2-4 years  
**Investigators:** Multiple  
**Sites:** Multicenter, North America, Europe, Latin America, Australia  
**Results/Publications:** Rationale and design described (Abstract #P02.150, AAN 2008)  
**Funding:** Genzyme Corporation, Bayer HealthCare Pharmaceuticals  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00548405>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Aspirin  
**Purpose of study:** To improve fatigue  
**Possible mechanism:** Inhibits prostaglandins  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Aspirin 81 mg bid po vs. aspirin 650 mg bid po vs. PBO po  
**Outcome parameters:** Modified Fatigue Impact Scale, Visual Analog Scale, cognitive fatigue measure, motor fatigue measure  
**Type of MS:** RR, SP  
**Number of Subjects:** 135  
**Start date:** March 2007  
**Observation period:** 8 weeks  
**Investigators:** D. Wingerchuk and others  
**Sites:** Mayo Clinic and Mayo Foundation, Scottsdale, AZ, Jacksonville, FL, Rochester, MN  
**Results/Publications:** Not available  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00467584>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Atacicept  
**Purpose of study:** To evaluate safety and effectiveness in reducing disease activity  
**Possible mechanism:** Blocks B cell maturation, function, survival  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Atacicept 150 mg biw sc (4 wks), then 150 mg/wk sc (32 wks) vs. atacicept 75 mg biw sc (4 wks), then 75 mg/wk sc (32 wks) + 25 mg biw sc (4 wks), then 25 mg/wk sc (32 wks) vs. PBO sc  
**Outcome parameters:** MRI, EDSS, MSFC  
**Type of MS:** RR  
**Number of Subjects:** 292  
**Start date:** June 2008  
**Observation period:** 48 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** EMD Serono  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00624468>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** ATL1102 **COMPLETED**

**Purpose of study:** To evaluate safety and MRI outcomes, and to determine the pharmacokinetic profile

**Possible mechanism:** Synthetic, second generation antisense oligonucleotide which acts as an inhibitor of VLA-4 mediated cell adhesion; targets alpha 4 integrin at the mRNA level, inhibiting protein translation and hence downregulation of VLA-4 surface expression

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** ATL1102 200 mg biw sc vs. PBO sc

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 77

**Start date:** 2006

**Observation period:** 16 weeks

**Investigators:** V. Limmroth and others

**Sites:** Multicenter, Central/Eastern Europe

**Results/Publications:** 54.4% reduction in cumulative number of new active lesions vs. PBO; 66.7% reduction in cumulative number of new T1-Gd lesions with ATL1102; adverse events in ATL1102 group included mild to moderate injection site reactions and a tendency for decreased platelet counts (reversible after treatment interruption) (Abstract #81, World Congress of MS 2008; Abstract #S11.001, AAN 2009)

**Funding:** Antisense Therapeutics

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Atorvastatin (Lipitor<sup>®</sup>, Pfizer Ireland Pharmaceuticals Corp.)

**Purpose of study:** To evaluate safety and effectiveness on decreasing or delaying clinical and MRI disease activity in patients with CIS

**Possible mechanism:** Promotes anti-inflammatory Th2 response

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 80 mg/d po vs. PBO po

**Outcome parameters:** Neurological and functional assessment tests, MRI, measure of metabolites

**Type of MS:** First clinical demyelinating event suggestive of MS

**Number of Subjects:** 83

**Start date:** January 2005

**Observation period:** 18 months

**Investigators:** S. Zamvil and others

**Sites:** University of California, San Francisco, and others, United States and Canada

**Results/Publications:** Not available

**Funding:** Immune Tolerance Network, National Institute of Allergy and Infectious Disease

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00094172>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Atorvastatin (Lipitor<sup>®</sup>, Pfizer Ireland Pharmaceuticals Corp.) and interferon beta-1a (Rebif<sup>®</sup>, Serono Pfizer)

**Purpose of study:** To delay time to definite MS in patients with CIS

**Possible mechanism:** Promotes anti-inflammatory Th2 response (Lipitor)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Rebif 44 mcg tiw sc + Lipitor 80 mg/d po vs. Rebif + PBO po

**Outcome parameters:** Gene expression, safety, efficacy

**Type of MS:** First clinical demyelinating event suggestive of MS

**Number of Subjects:** 30

**Start date:** October 2004

**Observation period:** 15 months

**Investigators:** S. Markovic-Plese

**Sites:** University of North Carolina, Chapel Hill

**Results/Publications:** Not available

**Funding:** University of North Carolina, Chapel Hill

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00137176>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** ATX-MS1467 **COMPLETED**

**Purpose of study:** To assess safety and tolerability

**Possible mechanism:** Induction of immunological tolerance with MBP-derived peptide

**Study description:** Open label, dose escalation

**Dose/route:** ATX-MS1467 25, 50, 100, 400 and 800 mcg given to each patient at 7- to 14-day intervals

**Outcome parameters:** Safety and immunological analysis of blood samples in vitro

**Type of MS:** SP

**Number of Subjects:** 6

**Start date:** 2006

**Observation period:** 3 months

**Investigators:** N. Scolding

**Sites:** University of Bristol, UK

**Results/Publications:** Safe and well tolerated; 4 patients displayed significant response to MBP at baseline that was suppressed at one-month follow up (Abstract #P533, World Congress of MS 2008)

**Funding:** Apitope Technology (Bristol) Ltd

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** AVP-923 (Zenvia™, Avanir Pharmaceuticals)  
**Purpose of study:** To improve pseudobulbar affect (pathological laughing/crying)  
**Possible mechanism:** Dextromethorphan/quinidine capsules, Antagonist of NMDA receptor, suppresses excitatory neurotransmitters  
**Study description:** Open label  
**Dose/route:** 1 capsule bid po for 12 wks vs. PBO bid po  
**Outcome parameters:** Emotional lability scale, patient diary, Visual Analog Scale, Pain Intensity Rating Scale  
**Type of MS:** All types, with pseudobulbar affect  
**Number of Subjects:** 600  
**Start date:** February 2003  
**Observation period:** 12 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** 506 enrolled with MS and 29 other neurological conditions; adverse events included nausea (23.9%), headache (22.3%), dizziness (18.8%), diarrhea (16.2%), and fatigue (13.8%), mostly mild to moderate in nature; electrocardiographic results suggested no clinically meaningful effect on cardiac repolarization (Abstract #P01.015, AAN 2007)  
**Funding:** Avanir Pharmaceuticals  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00056524>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** AVP-923 (Zenvia™, Avanir Pharmaceuticals)  
**Purpose of study:** To improve pseudobulbar affect (pathological laughing/crying)  
**Possible mechanism:** Dextromethorphan/quinidine capsules, Antagonist of NMDA receptor, suppresses excitatory neurotransmitters  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 30 (dextromethorphan)/10 (quinidine) capsules bid po for 12 wks vs. 20/10 capsules bid po vs PBO bid po  
**Outcome parameters:** Patient record of PBA episodes  
**Type of MS:** All types, with pseudobulbar affect  
**Number of Subjects:** 306  
**Start date:** December 2007  
**Observation period:** 168 days  
**Investigators:** Multiple  
**Sites:** Multicenter, United States and Latin America  
**Results/Publications:** Not available  
**Funding:** Avanir Pharmaceuticals  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00573443>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** BAF312

**Purpose of study:** To test safety and effect on disease activity

**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue

**Study description:** Randomized, double blinded, placebo controlled, dose ranging

**Dose/route:** BAF312 0.5 mg/d po vs. BAF312 2.0 mg/d po vs. BAF312 10.0 mg/d po vs. PBO po; then dose adjustment for active arms vs. PBO

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 31, then 19

**Start date:** May 2009

**Observation period:** Not available

**Investigators:** Not available

**Sites:** Not available

**Results/Publications:** Not available

**Funding:** Novartis

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** BG00012 (dimethyl fumarate)

**COMPLETED**

**Purpose of study:** To test safety and effectiveness in controlling disease course and development of brain lesions

**Possible mechanism:** Upregulates Th2 response, immunomodulatory

**Study description:** Double blinded, placebo controlled

**Dose/route:** 120 mg/d po vs. 120 mg tid po vs. 240 mg tid po vs. PBO

**Outcome parameters:** MRI, relapse rate, EDSS

**Type of MS:** RR

**Number of Subjects:** 260

**Start date:** November 2005

**Observation period:** 24 weeks + 24-week extension

**Investigators:** L. Kappos and others

**Sites:** Multicenter, worldwide

**Results/Publications:** BG00012 240 mg tid reduced Gd lesions by 69% compared with PBO and number of new or enlarging T2 and new T1 lesions by 32% compared with PBO; BG00012 reduced relapse rate, but not significantly; abdominal pain, flushing, and hot flush more common in BG00012 group; dose-related adverse events include headache, fatigue, and feeling hot (*Lancet* 2008 Oct 25;372(9648):1463-72)

**Funding:** Biogen Idec, Inc., Fumapharm AG

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00168701>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** BG00012 (dimethyl fumarate)

**Purpose of study:** To test safety and effectiveness in controlling disease course and development of brain lesions, also known as DEFINE study

**Possible mechanism:** Upregulates Th2 response, immunomodulatory

**Study description:** Double blinded, placebo controlled

**Dose/route:** 480 mg/d po vs. 720 mg/d po vs. PBO po

**Outcome parameters:** Proportion of relapsing patients, frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** RR

**Number of Subjects:** 1011

**Start date:** March 2007

**Observation period:** 2 years

**Investigators:** Multiple

**Sites:** Multicenter, worldwide

**Results/Publications:** Not available

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00420212>

**Last update:** 2008

\*\*\*\*\*

**Agent:** BG00012 (dimethyl fumarate) vs. glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries, Ltd.)

**Purpose of study:** To test safety and effectiveness in controlling disease course and development of brain lesions, also known as CONFIRM study

**Possible mechanism:** Upregulates Th2 response, immunomodulatory (BG0012)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

**Study description:** Double blinded, placebo controlled

**Dose/route:** BG00012 480 mg/d po vs. 720 mg/d po vs. Copaxone 20 mg/d sc vs. PBO po

**Outcome parameters:** Proportion of relapsing patients, frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** RR

**Number of Subjects:** 1232

**Start date:** July 2007

**Observation period:** 2 years

**Investigators:** Multiple

**Sites:** Multicenter, worldwide

**Results/Publications:** Not available

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00451451>

**Last update:** 2008

\*\*\*\*\*

**Agent:** BHT-3009 **COMPLETED**

**Purpose of study:** To evaluate safety and effectiveness and to confirm effects on immune tolerance

**Possible mechanism:** DNA vaccine designed to induce tolerance to myelin basic protein

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** BHT-3009 0.5 mg im vs. BHT-3009 1.5 mg im vs. PBO im at weeks 0, 2, 4, and every 4 weeks thereafter until week 44

**Outcome parameters:** MRI, relapse rate, MSFC, anti-myelin autoantibodies

**Type of MS:** RR

**Number of Subjects:** 267

**Start date:** February 2006

**Observation period:** 48 weeks

**Investigators:** Multiple

**Sites:** Multicenter, Europe, Asia, and North America

**Results/Publications:** Median 4-week rate of new enhancing lesions during weeks 28 to 48 was 50% lower with 0.5 mg BHT-3009 and during weeks 8 to 48 was 61% lower with 0.5 mg BHT-3009; mean volume of enhancing lesions at week 48 was 51% lower on 0.5mg BHT-3009 compared with PBO; relapse rates not significantly different during treatment period, but relapse rate decreased significantly in follow-up 7 months after last dose in 0.5-mg group and returned to previous rate at 13 months (*Annals of Neurology* 2008;63:611–620; Abstract #P07.142, AAN 2009)

**Funding:** Bayhill Therapeutics, Inc.

**ClinicalTrials.gov Link:**

**Last Update:** 2009

\*\*\*\*\*

**Agent:** BHT-3009 + atorvastatin (Lipitor<sup>®</sup>, Pfizer Ireland) **COMPLETED**

**Purpose of study:** To control disease course and development of brain lesions

**Possible mechanism:** DNA vaccine designed to induce tolerance to myelin basic protein (BHT-3009-01)/Promotes Th2 response (Lipitor)

**Study description:** Double blinded, crossover

**Dose/route:** BHT-3009 or PBO im in weeks 1, 3, 5, 9; Lipitor 80 mg/d or PBO po/d for weeks 1-13; patients who initially receive PBO will subsequently receive Rx

**Outcome parameters:** EDSS, MRI

**Type of MS:** RR, SP

**Number of Subjects:** 30

**Start date:** July 2004

**Observation period:** 1 year

**Investigators:** T. Vollmer and others

**Sites:** Barrow Neurological Institute, St. Joseph's Hospital, Phoenix, AZ, and others

**Results/Publications:** Well tolerated; marked decrease in IFN gamma-producing, myelin reactive CD4+ T cells; favorable but insignificant trends on MRI (*Archives of Neurology* 2007; 64: 1407-1415)

**Funding:** Bayhill Therapeutics, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00103974>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Bone marrow/peripheral stem cell transplantation (autologous)  
**Purpose of study:** To control development of brain lesions, also known as MIST study  
**Possible mechanism:** Rids the body of T cells that drive the immune attack against CNS  
**Study description:** Open, crossover  
**Dose/route:** Cyclophosphamide 60 mg/kg/d for 2 days iv + rATG .5 mg/kg on day -5, 1 mg/kg on day -4, and 1.5 mg/kg on days -3,-2,-1 iv vs. standard therapy (interferons, Copaxone<sup>®</sup> or mitoxantrone)  
**Outcome parameters:** EDSS, number of relapses, ambulation index, timed ambulation, 9-hole peg test, PASAT, MRI, SF-36, Multiple Sclerosis International Quality of Life Questionnaire, Neurological Rating Scale, survival  
**Type of MS:** RR, active  
**Number of Subjects:** 110  
**Start date:** January 2006  
**Observation period:** 5 years  
**Investigators:** R. Burt and others  
**Sites:** Northwestern University Feinberg School of Medicine, Chicago, and others  
**Results/Publications:** Not available  
**Funding:** Not available  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00273364>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Bone marrow/peripheral stem cell transplantation (autologous)  
**Purpose of study:** To control development of brain lesions, also known as HALT MS study  
**Possible mechanism:** Rids the body of T cells that drive the immune attack against CNS  
**Study description:** Open label  
**Dose/route:** Carmustine 300 mg/m<sup>2</sup> iv, etoposide 100 mg/m<sup>2</sup> iv, cytarabine 100 mg/m<sup>2</sup> iv, melphalan 140 mg/m<sup>2</sup> iv, thymoglobulin 3.5 mg/kg iv, granulocyte-colony stimulating factor 5 mcg/kg/d sc, prednisone .5 mg/kg iv  
**Outcome parameters:** EDSS, MSFC, MRI, relapse  
**Type of MS:** RR, PR  
**Number of Subjects:** 30  
**Start date:** June 2006  
**Observation period:** 5 years  
**Investigators:** R. Nash and others  
**Sites:** Fred Hutchinson National Cancer Center, Seattle, and others  
**Results/Publications:** First 7 people followed for average of 9.5 months; no further relapses; EDSS stable (n=2), improved (n=3), worsened by 0.5 (n=1); no new/enhancing lesions; one case each of graft-versus-host disease, pseudo-relapse and MRSA infection occurred transiently (Abstract #P02.179, AAN 2008; Abstract #P07.133, AAN 2009)  
**Funding:** National Institute of Allergy and Infectious Disease  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00288626>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Bone marrow/peripheral stem cell transplantation (autologous)  
**Purpose of study:** To control disease course and development of brain lesions  
**Possible mechanism:** Rids the body of T cells that drive the immune attack against CNS  
**Study description:** Open study  
**Dose/route:** Stem cell mobilization with cyclophosphamide 4.5 g/m<sup>2</sup> iv + G-CSF 10 g/kg/d G-CSF sc for 10 days; immunoablation with cyclophosphamide, busulfan, rATG  
**Outcome parameters:** Clinical, MRI, immune function  
**Type of MS:** Rapidly progressive  
**Number of Subjects:** 24  
**Start date:** February 2001  
**Observation period:** 1-8 years  
**Investigators:** M. Freedman and others  
**Sites:** University of Ottawa and others  
**Results/Publications:** 6/16 patients with  $\geq 1.5$  year of follow-up showed sustained EDSS improvements (3/16 worsened and 7/16 unchanged compared with baseline); those showing earliest changes also had shortest disease course; no Gd enhancing lesions; T2 lesion volumes remained stable in 7/16 (Abstract #P06.077, AAN 2002; Abstract #S11.006, AAN 2003; Abstracts #S60.005 and #S40.005, AAN 2004; Abstracts #S46.005 and #S46.006, AAN 2005; Abstract #SC2.013, AAN 2006; Abstract #73, ECTRIMS 2007; Abstract P02.145, AAN 2009)  
**Funding:** MS Scientific Research Foundation  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Botulinum toxin A (Botox<sup>®</sup>, Allergan, Inc.) **TERMINATED**  
**Purpose of study:** To improve spasticity  
**Possible mechanism:** Blocks neuromuscular transmission  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Botox 50-100 units per muscle im, depending on severity of spasticity and muscle size  
**Outcome parameters:** Quality of life, functional assessments, pain assessments, spasticity measures  
**Type of MS:** All types  
**Number of Subjects:** 40  
**Start date:** September 2005  
**Observation period:** 12 weeks  
**Investigators:** J. Preiningerova, B. Jabbari  
**Sites:** Yale Center for MS Treatment and Research, New Haven, CT  
**Results/Publications:** Ended early due to difficulty recruiting patients (Communication with primary investigator)  
**Funding:** Allergan, Inc.  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Botulinum toxin A (Botox<sup>®</sup>, Allergan, Inc.)  
**Purpose of study:** To improve bladder dysfunction, also known as Dignity Study  
**Possible mechanism:** Blocks neuromuscular transmission  
**Study description:** Double blinded, placebo controlled, parallel-group study  
**Dose/route:** Botox 200 units injected into bladder vs. Botox 300 units injected into bladder vs. PBO injected into bladder, at least 12 wks apart  
**Outcome parameters:** Number of incontinence episodes  
**Type of MS:** All types, stable for  $\geq 3$  mos; EDSS  $\leq 6.5$   
**Number of Subjects:** 405  
**Start date:** August 2006  
**Observation period:** up to 3 years  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** Allergan, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00311376>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Botulinum toxin A (Botox<sup>®</sup>, Allergan, Inc.)  
**Purpose of study:** To improve bladder and respiratory dysfunction, also known as Dignity TOO Study  
**Possible mechanism:** Blocks neuromuscular transmission  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Botox 200 units injected into bladder vs. Botox 300 units injected into bladder vs. PBO injected into bladder; up to 2 treatments 12 wks apart  
**Outcome parameters:** Number of incontinence episodes, safety, pulmonary function  
**Type of MS:** All types, stable for  $\geq 3$  mos; EDSS  $7.0 \leq 8.0$   
**Number of Subjects:** 135  
**Start date:** May 2007  
**Observation period:** up to 52 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** Allergan, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00439140>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** C-105 (l amphetamine sulfate)  
**Purpose of study:** To evaluate effects on cognitive function  
**Possible mechanism:** Central nervous system stimulant  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** C-105 5 mg/d po titrated to 30 mg/d po over one month vs. PBO po  
**Outcome parameters:** Safety, cognitive testing  
**Type of MS:** RR, SP, with cognitive dysfunction  
**Number of Subjects:** 151  
**Start date:** 2006  
**Observation period:** 1.5 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Primary outcomes (processing speed and executive function) not met; significant improvement in secondary outcomes (learning and memory) at highest dose (30 mg/d); limited side-effect profile (Press release, Cognition Pharmaceuticals, December 17, 2008)  
**Funding:** Cognition Pharmaceuticals  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00529581>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Cannabis extract (cannador)  
**Purpose of study:** To improve pain and muscle stiffness, also known as MUSEC trial  
**Possible mechanism:** May inhibit neurotransmitter release, affect immune function, be neuroprotective  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Cannador 5 mg/d po (individual dose titration of 5 mg every 3 days to 25 mg/d, administered as 2 equal doses based on tolerability) vs. PBO po  
**Outcome parameters:** Likert Scale (pain severity)  
**Type of MS:** All types, stable for at least 6 mos  
**Number of Subjects:** 400  
**Start date:** June 2006  
**Observation period:** 12 weeks  
**Investigators:** J. Zajicek and others  
**Sites:** Peninsula Medical School, Plymouth, and others, United Kingdom  
**Results/Publications:** Not available  
**Funding:** Weleda AG and IKF  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00552604>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Cannabis extract (dronabinol vs. cannabis)  
**Purpose of study:** To improve spasticity  
**Possible mechanism:** Interacts with cannabinoid receptors on CNS cells, possibly impacting motor function, cognition and affect  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** 1 cannabis cigarette per day + PBO po vs. dronabinol 10 mg/d po + smoked PBO vs. smoked PBO + PBO po  
**Outcome parameters:** EDSS, Lido measurement of spasticity, Ashworth, MSFC, MSQLI  
**Type of MS:** SP, PP  
**Number of Subjects:** 60  
**Start date:** April 2004  
**Observation period:** Up to 5 months  
**Investigators:** M. Agius and D. Richman  
**Sites:** UC Davis Medical Center  
**Results/Publications:** Not available  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00260741>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Cannabis extract (dronabinol)  
**Purpose of study:** To determine ability to prevent disease progression, also known as CUPID trial  
**Possible mechanism:** May reduce neuronal damage mediated through an interaction with cannabinoid type 1 and opioid receptors  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** Dronabinol 3.5-28 mg/d po in two divided doses titrated according to body weight and adverse events vs. PBO po  
**Outcome parameters:** EDSS, MSIS-29 physical impact scale  
**Type of MS:** PP, SP  
**Number of Subjects:** 492  
**Start date:** May 2006  
**Observation period:** 3 years  
**Investigators:** J. Zajicek and others  
**Sites:** Peninsula Medical School, Plymouth, and others, United Kingdom  
**Results/Publications:** Not available  
**Funding:** Medical Research Council (UK), MS Society (UK) and MS Trust (UK)  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Cannabis extract (tetrahydrocannabinol and cannabidiol, Sativex<sup>®</sup>, GW Pharm.)  
**Purpose of study:** To improve pain  
**Possible mechanism:** Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can gradually self-titrate to maximum of 24 sprays in 24 hrs  
**Outcome parameters:** Pain (Numeric Rating Scale), Neuropathic Pain Scale, QOL, safety  
**Type of MS:** All types, with central neuropathic pain  
**Number of Subjects:** 339  
**Start date:** July 2006  
**Observation period:** 15 weeks  
**Investigators:** Multiple  
**Sites:** Multiple, Canada and Europe  
**Results/Publications:** In preliminary results, 50% of Sativex group had pain reduction of at least 30%, but primary/secondary endpoints not statistically significant possibly due to large placebo response (GW Pharmaceuticals press release, April 8, 2008)  
**Funding:** GW Pharmaceuticals, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00391079>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Cannabis extract (tetrahydrocannabinol and cannabidiol, Sativex<sup>®</sup>, GW Pharmaceuticals) **COMPLETED**  
**Purpose of study:** To improve spasticity  
**Possible mechanism:** Interacts with cannabinoid receptors on CNS cells, possibly relating to motor function, cognition and affect  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 100 microliters of tetrahydrocannabinol/cannabidiol per spray, directed under tongue or inside cheeks; patients can gradually self-titrate to a maximum of 12 sprays in 24 hours vs. PBO  
**Outcome parameters:** Numerical Rating Scale and other scales  
**Type of MS:** RR, P, with spasticity  
**Number of Subjects:** 572  
**Start date:** January 2008  
**Observation period:** 56 weeks  
**Investigators:** Multiple  
**Sites:** Multiple, Europe  
**Results/Publications:** 241 patients responded to 4 weeks of treatment and entered 2nd phase of 12 weeks; 74% achieved improvement of greater than 30% in spasticity score vs. 51% on PBO; statistically significant improvements were also seen in spasm frequency, sleep disturbance, patient global impression of change, and physician global impression of change (GW Pharmaceuticals press release, March 11, 2009)  
**Funding:** GW Pharmaceuticals, Inc.  
**ClinicalTrials.gov Identifier:** <http://clinicaltrials.gov/ct2/showNCT00681538>  
**Last update:** 2009

\*\*\*\*\*

**Agent:** CDP323

**Purpose of study:** To evaluate safety, tolerability and effects of two doses

**Possible mechanism:** VLA-4 inhibitor, blocking entry of immune cells into CNS

**Study description:** Double blinded, placebo controlled

**Dose/route:** CDP323 500 mg bid po vs. CDP323 250 mg bid po vs. PBO po

**Outcome parameters:** MRI

**Type of MS:** RR, SP with superimposed relapses

**Number of Subjects:** 225

**Start date:** May 2007

**Observation period:** 40 weeks

**Investigators:** Multiple

**Sites:** Multicenter, US and Europe

**Results/Publications:** Not available

**Funding:** UCB and Biogen Idec

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00484536>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Chaperonin 10

**COMPLETED**

**Purpose of study:** To assess safety, tolerability and pharmacodynamics

**Possible mechanism:** Suppression of innate immunity via toll-like receptors

**Study description:** Double blinded, placebo controlled

**Dose/route:** 5 mg/wk iv vs. 5 mg biw iv vs. PBO iv

**Outcome parameters:** Frequency of relapse, EDSS, MRI

**Type of MS:** RR,SP

**Number of Subjects:** 50

**Start date:** March 2005

**Observation period:** 20 weeks

**Investigators:** S. Broadley and others

**Sites:** Multicenter, Australia

**Results/Publications:** No significant differences in frequency of adverse events; no difference in clinical outcome measures; trend to improvement in Gd lesions in chaperonin 10 group (*Multiple Sclerosis* 2009 Mar;15(3):329-36)

**Funding:** CBio Ltd. Brisbane

**ClinicalTrials.gov Link:** Australian Clinical Trials Registry (ACTRNO 12606000037505)

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Cladribine **COMPLETED**  
**Purpose of study:** To test safety, effectiveness, also known as CLARITY study  
**Possible mechanism:** Lymphocyte reduction  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Cladribine 0.875 mg/kg/cycle po over 5 days per month, administered in 2 or 4 cycles per year vs. PBO po  
**Outcome parameters:** Relapse rate, EDSS, MRI  
**Type of MS:** RR  
**Number of Subjects:** 1326  
**Start date:** April 2005  
**Observation period:** 2 years  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Relapse rate reduced by 58% (low-dose) and 55% (high-dose) vs. PBO; proportion of relapse-free patients significantly higher in Rx groups vs. PBO; Rx groups had more than 30% reduction in risk of disability progression (EDSS) vs. PBO and at least 70% reduction in mean number of Gd lesions, active T2 lesions, and combined unique lesions; 4 malignancies (cervical stage 0, melanoma, ovarian and pancreatic) and 1 case of choriocarcinoma (in pregnancy 6 months post-study) reported in Rx groups; common adverse events were headaches, upper respiratory tract infections, nasopharyngitis, nausea, and lymphopenia; herpes zoster in 2.3% of Rx groups (Abstract #LBS.001, AAN 2009)  
**Funding:** EMD Serono, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00213135>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Cladribine + interferon beta-1a (Rebif® [fetal bovine serum-free/human serum albumin-free formulation], Serono Pfizer)  
**Purpose of study:** To test safety, effectiveness, also known as ONWARD study  
**Possible mechanism:** Lymphocyte reduction (Cladribine)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Cladribine 0.875 mg/kg/cycle po for two cycles + Rebif 44 mcg tiw sc vs. Cladribine 0.875 mg/kg/cycle po for four cycles + Rebif 44 mcg tiw sc vs. Rebif + PBO po  
**Outcome parameters:** EDSS, MRI, safety  
**Type of MS:** Relapsing forms  
**Number of Subjects:** 260  
**Start date:** December 2006  
**Observation period:** 104 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Rationale and design described (Abstract #P809, ECTRIMS 2007)  
**Funding:** EMD Serono, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00436826>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** CNTO 1275 (monoclonal antibody)  
**Purpose of study:** To test safety, impact on immune function  
**Possible mechanism:** Blocks IL-12 cytokine activity  
**Study description:** Randomized, double blinded, placebo controlled, dose ranging  
**Dose/route:** 30-200 mg monthly or bimonthly sc vs. PBO  
**Outcome parameters:** MRI  
**Type of MS:** RR  
**Number of Subjects:** 250  
**Start date:** July 2004  
**Observation period:** 71 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter  
**Results/Publications:** Not available  
**Funding:** Centocor, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00207727>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Cyclophosphamide **COMPLETED**  
**Purpose of study:** To test safety and control disease progression, development of lesions  
**Possible mechanism:** Alkylating agent, interferes with proliferating immune cells  
**Study description:** Pilot, open label  
**Dose/route:** 50 mg/kg/d iv for 4 days  
**Outcome parameters:** Frequency of relapse, scoring technique, MRI  
**Type of MS:** Aggressive RR  
**Number of Subjects:** 9  
**Start date:** October 2003  
**Observation period:** 2 years  
**Investigators:** D. Kerr and others  
**Sites:** Johns Hopkins University, Baltimore  
**Results/Publications:** 9 patients were treated and followed up for mean of 23 months; all developed transient total or near-total pancytopenia followed by hematopoietic recovery in 10-17 days; statistically significant reduction in disability (EDSS) and in mean number of Gd lesions at follow-up; 2 patients required rescue treatment with other immunomodulatory therapies during the study due to MS relapse (*Archives of Neurology* 2008;65(8):1044-51)  
**Funding:** Johns Hopkins GCRC  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2009

\*\*\*\*\*

**Agent:** Cyclophosphamide vs. methylprednisolone  
**Purpose of study:** To control disease progression, also known as PROMESS study  
**Possible mechanism:** Alkylating agent, interferes with rapidly proliferating immune cells (cyclophosphamide)/Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)  
**Study description:** Randomized, double blinded  
**Dose/route:** Cyclophosphamide 750 mg/m<sup>2</sup> (if lymphocytes >1400) or 500 mg/m<sup>2</sup> (if lymphocytes <1400 and > 1000) or 400 mg/m<sup>2</sup> (if lymphocytes <900) every 4 wks for yr 1 and every 8 wks for yr 2 iv + ondansetron vs. methylprednisolone 1 g every 4 wks for yr 1 and every 8  
**Outcome parameters:** EDSS, MSFC, frequency of relapse  
**Type of MS:** SP  
**Number of Subjects:** 360  
**Start date:** November 2005  
**Observation period:** 2 years  
**Investigators:** B. Brochet and others  
**Sites:** Multicenter, France  
**Results/Publications:** Not available  
**Funding:** French Health Ministry  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00241254>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Daclizumab  
**Purpose of study:** To evaluate safety and effectiveness, also known as CHOICE trial  
**Possible mechanism:** Limits T cell expansion by blocking signaling of cytokine IL-2  
**Study description:** Randomized, double blinded, placebo controlled, dose ranging  
**Dose/route:** 2 mg/kg sc every 2 wks vs. 1 mg/kg sc every 4 wks (alternates with PBO every 2 weeks) vs. PBO sc  
**Outcome parameters:** Gd-MRI lesions, relapse rate, EDSS, MSFC  
**Type of MS:** Active, relapsing  
**Number of Subjects:** 270  
**Start date:** April 2005  
**Observation period:** 72 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, United States, Canada, Europe  
**Results/Publications:** Gd-MRI lesions significantly reduced by 72% in the high-dose group compared with PBO; low-dose grouped showed a 25% reduction compared with PBO, not statistically significant (Abstract #50,ECTRIMS 2007; Abstract #PL01.003, AAN 2008)  
**Funding:** Biogen Idec, Inc., PDL BioPharma, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00109161>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Daclizumab  
**Purpose of study:** To evaluate safety and effectiveness, also known as ZAP MS study  
**Possible mechanism:** Limits T cell expansion by blocking signaling of cytokine IL-2  
**Study description:** Open label  
**Dose/route:** 1 mg/kg/mo iv  
**Outcome parameters:** MRI, clinical and immunological parameters  
**Type of MS:** RR  
**Number of Subjects:** 15  
**Start date:** January 2004  
**Observation period:** 20.5 months  
**Investigators:** H. McFarland and others  
**Sites:** National Institutes Health, Bethesda, MD  
**Results/Publications:** Not available  
**Funding:** NIH Intramural Research  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00071838>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Donepezil (Aricept<sup>®</sup>, Eisai Co.)  
**Purpose of study:** To improve memory, also known as AIMS study  
**Possible mechanism:** Cholinesterase inhibitor  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Aricept 5 mg/d po for 4 wks, then 10 mg/d for 20 wks vs. PBO po  
**Outcome parameters:** Selective Reminding Test  
**Type of MS:** All types  
**Number of Subjects:** 144  
**Start date:** Spring 2005  
**Observation period:** 24 weeks  
**Investigators:** L. Krupp and others  
**Sites:** SUNY Stony Brook, NY, and others  
**Results/Publications:** Not available  
**Funding:** NIH  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00062972>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Doxycycline + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)

**COMPLETED**

**Purpose of study:** To test safety and control disease activity

**Possible mechanism:** Synthetic tetracycline derivative that inhibits matrix metalloproteinases (doxycycline)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Open label

**Dose/route:** Avonex 30 mcg/wk im + doxycycline 100 mg/d po

**Outcome parameters:** Frequency of relapse, MRI, other

**Type of MS:** RR

**Number of Subjects:** 15

**Start date:** Not available

**Observation period:** 6 months

**Investigators:** A. Minagar

**Sites:** LSU-HSC Shreveport, LA

**Results/Publications:** Combination treatment resulted in reductions in contrast-enhancing lesion numbers and EDSS; 1 patient relapsed; correlations between decreased serum matrix metalloproteinase-9 levels and enhancing lesion activity reduction; adverse effects mild (*Archives of Neurology* 2008 Feb;65(2):199-204)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00246324>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Duloxetine hydrochloride (Cymbalta<sup>®</sup>, Lilly)

**Purpose of study:** To decrease central neuropathic pain due to MS.

**Possible mechanism:** Inhibits serotonin and norepinephrine reuptake in CNS, leading to modulation of central sensitization and neuroplasticity

**Study description:** Double blinded, placebo controlled

**Dose/route:** 60 mg/d po for 6 wks followed by 60, 90, or 120 mg/d po for up to 12 wks vs. PBO

**Outcome parameters:** Likert Scale (pain severity)

**Type of MS:** All types, with central neuropathic pain

**Number of Subjects:** 238

**Start date:** November 2008

**Observation period:** Up to 20 weeks

**Investigators:** Multiple

**Sites:** Multicenter, worldwide

**Results/Publications:** Not available

**Funding:** Eli Lilly and Company

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00755807>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Estriol  
**Purpose of study:** To control disease course  
**Possible mechanism:** Pregnancy hormone that decreases Th1 inflammatory immune response  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Estriol 8 mg/d po + Copaxone 20 mg/d sc vs Copaxone + PBO  
**Outcome parameters:** Relapse rate, MSFC, EDSS, MRI  
**Type of MS:** RR, women  
**Number of Subjects:** 130  
**Start date:** June 2007  
**Observation period:** 2 years  
**Investigators:** R. Voskuhl and others  
**Sites:** University of California at Los Angeles and others, United States  
**Results/Publications:** Not available  
**Funding:** National MS Society, NIH, others  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00451204>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fampridine-SR (4-aminopyridine, sustained release) **COMPLETED**  
**Purpose of study:** To test safety and effectiveness in improvement of walking ability in people with MS  
**Possible mechanism:** Blocks potassium channels on axons, permitting demyelinated axon to transmit impulses  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** po  
**Outcome parameters:** Timed 25-Foot Walk  
**Type of MS:** All types  
**Number of Subjects:** 200  
**Start date:** June 2007  
**Observation period:** 14 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, United States and Canada  
**Results/Publications:** 43% of those on treatment showed consistent improvement in walking speed, versus about 9% of those on PBO; among responders, speed improved by about 25% from baseline; one patellar fracture in fampridine group led to discontinuation (Abstract #P909, World Congress of MS, 2008)  
**Funding:** Acorda Therapeutics, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00483652>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fingolimod (FTY720) **COMPLETED**  
**Purpose of study:** To test safety, effectiveness on reduction of relapses and brain lesions  
**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** 1.25 mg po vs 5 mg po vs PBO po for 6 mos; in 6-mo extension, those on PBO randomized to 1.25 mg po vs 5 mg po  
**Outcome parameters:** Frequency of relapse, MRI  
**Type of MS:** RR  
**Number of Subjects:** 255  
**Start date:** 2004  
**Observation period:** 6 months, with 18-month extension  
**Investigators:** L. Kappos and others  
**Sites:** Multicenter, Europe and Canada  
**Results/Publications:** At 36 months (30-month extension study), 173 participants remaining on fingolimod continued to show sustained annualized relapse rate; 89% remain free of Gd-enhancing lesions; no T2 activity in 75%; most frequently reported adverse events were nasopharyngitis, influenza, headache and fatigue; 20-24% of patients met 6-month confirmed disability progression on EDSS (*New England Journal of Medicine* 2006;355(11):1124-40; Abstract #P06.085, AAN 2007; Abstract #S12.005, AAN 2008)  
**Funding:** Novartis  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Fingolimod (FTY720)  
**Purpose of study:** To test safety and effectiveness, also known as FREEDOMS study  
**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 0.5 mg/d po vs. 1.25 mg/d po vs PBO  
**Outcome parameters:** Frequency of relapse, disability progression, MRI, safety  
**Type of MS:** RR  
**Number of Subjects:** 1272  
**Start date:** January 2006  
**Observation period:** 2 years  
**Investigators:** L. Kappos and others  
**Sites:** Multicenter, Europe and North America  
**Results/Publications:** Baseline information on 1272 participants (Abstract #P73, World Congress of MS 2008)  
**Funding:** Novartis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00289978>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fingolimod (FTY720)  
**Purpose of study:** To test safety and effectiveness, also known as FREEDOMS II study  
**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 0.5 mg/d po vs. 1.25 mg/d po vs PBO po  
**Outcome parameters:** Frequency of relapse  
**Type of MS:** RR  
**Number of Subjects:** 1080  
**Start date:** June 2006  
**Observation period:** 24 months  
**Investigators:** D. Huang and others  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** Novartis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00355134>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fingolimod (FTY720)  
**Purpose of study:** To test safety and effectiveness, also known as INFORMS study  
**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** 1.25 mg/d po vs PBO po  
**Outcome parameters:** Scoring technique, MRI, frequency of relapse  
**Type of MS:** PP  
**Number of Subjects:** 100  
**Start date:** January 2009  
**Observation period:** 3-4.5 years  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** Novartis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00731692>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fingolimod (FTY720) vs. Avonex<sup>®</sup> (interferon beta-1a, Biogen Idec)  
**Purpose of study:** To test safety and effectiveness, also known as TRANSFORMS study  
**Possible mechanism:** Sphingosine-1-phosphate receptor binder; prevents lymphocytes from exiting lymphatic tissue (fingolimod)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (  
**Study description:** Randomized, double blinded, parallel group  
**Dose/route:** 0.5 mg/d po vs. 1.25 mg/d po vs Avonex 30 mcg/wk im  
**Outcome parameters:** Frequency of relapse  
**Type of MS:** RR  
**Number of Subjects:** 1292  
**Start date:** May 2006  
**Observation period:** 12 months  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Annualized relapse rate reduced by 52% in fingolimod .5-mg group and by 38% in 1.25-mg group compared to Avonex (Novartis press release, December 12, 2008; Abstract #S21.004, AAN 2009)  
**Funding:** Novartis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00340834>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Fish oil  
**Purpose of study:** To improve depression  
**Possible mechanism:** Decreases cytokine levels  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** 3 g bid po vs. PBO po  
**Outcome parameters:** Becks Depression Inventory, Montgomery-Asberg Depression Rating Scale, cytokine measurements, red blood cell fatty acid analysis  
**Type of MS:** All types  
**Number of Subjects:** 60  
**Start date:** August 2005  
**Observation period:** 6 months  
**Investigators:** L. Shinto, D. Bourdette  
**Sites:** Oregon Health & Science University, Portland  
**Results/Publications:** Not available  
**Funding:** NIH  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00122954>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Ginkgo biloba  
**Purpose of study:** To improve cognitive function  
**Possible mechanism:** Alter neural function  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** 120 mg bid po vs. PBO po  
**Outcome parameters:** Battery of neuropsychological tests  
**Type of MS:** RR, P  
**Number of Subjects:** 158  
**Start date:** January 2009  
**Observation period:** 12 weeks  
**Investigators:** D. Bourdette, J. Haselkorn  
**Sites:** Portland VA Medical Center, VA Puget Sound Health Care System  
**Results/Publications:** Not available  
**Funding:** VA Rehabilitation Research and Development Service  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00841321>  
**Last Update:** 2009  
\*\*\*\*\*

**Agent:** Ginseng  
**Purpose of study:** To improve mental alertness and fatigue  
**Possible mechanism:** Possible glucoregulatory and/or immunoregulatory properties  
**Study description:** Double blinded, placebo controlled, crossover  
**Dose/route:** 100 mg/d po increased to 400 mg/d as tolerated vs. PBO po  
**Outcome parameters:** Activity Monitoring, Fatigue Severity Scale, Modified Fatigue Severity Scale, Beck Depression Inventory, Doodrill Stroop, Victoria Modified Stroop, MSFC, Sexual Function Questionnaire, Perceived Stress Scale, SF-36, Salivary Cortisol Levels  
**Type of MS:** All types  
**Number of Subjects:** 108  
**Start date:** October 2005  
**Observation period:** 17 weeks  
**Investigators:** R. Whitham, E. Kim  
**Sites:** Oregon Health & Science University, Portland  
**Results/Publications:** No significant improvement in primary or secondary endpoints (Abstract #S21.006, AAN 2009)  
**Funding:** CVT Technologies  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2009  
\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.)  
**Purpose of study:** Long-term follow up of patients in original trial  
**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2  
**Study description:** Prospective, open label, multi-year follow-up of patients in original study  
**Dose/route:** 20 mg/d sc  
**Outcome parameters:** EDSS  
**Type of MS:** RR  
**Number of Subjects:** 85  
**Start date:** 1991  
**Observation period:** Ongoing  
**Investigators:** K. Johnson and others  
**Sites:** Multicenter, United States  
**Results/Publications:** Study continues with 85 people still enrolled (*Multiple Sclerosis* 2006;12:309-320; communication with primary investigator)  
**Funding:** Teva Pharmaceutical Industries, Ltd.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00203021>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharm.Industries Ltd.) **COMPLETED**  
**Purpose of study:** To evaluate effectiveness in delaying conversion to clinically definite MS, also known as PreCISe Study  
**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** 20 mg/d sc vs. PBO sc  
**Outcome parameters:** Time to conversion to clinically definite MS, MRI  
**Type of MS:** First clinical demyelinating event suggestive of MS  
**Number of Subjects:** 480  
**Start date:** November 2003  
**Observation period:** 5 years  
**Investigators:** G. Comi and others  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Risk of developing clinically definite MS reduced by 45% versus PBO; time to development of definite MS delayed by 386 days compared to PBO; NAA levels significantly higher in people taking Copaxone in a subgroup of 34 people at 1 year; label extended to include CIS and MRI consistent with MS (Abstract #LBS.003, AAN 2008; Teva Pharmaceutical Industries press release, December 3, 2007; Abstracts #17, P32, P501, World Congress of MS 2008; Teva Pharmaceutical Industries press release, March 3, 2009)  
**Funding:** Teva Neuroscience  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) + albuterol (Proventil<sup>®</sup>, Schering Corporation) **COMPLETED**  
**Purpose of study:** To control disease course, development of lesions, immune function  
**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Decreases activity of cytokine IL-12 (Proventil)  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Copaxone 20 mg/d sc + albuterol 4 mg/d po vs. Copaxone + PBO po  
**Outcome parameters:** MSFC, time to relapse, number and severity of relapses, MRI, clinical scales, change in cytokine secretions and % of IL-12-producing monocytes  
**Type of MS:** RR  
**Number of Subjects:** 44  
**Start date:** September 2001  
**Observation period:** 2 years of follow-up  
**Investigators:** S. Khoury  
**Sites:** Brigham and Women's Hospital MS Center, Boston  
**Results/Publications:** Treatment effect at 6 months that diminished; trend for improved MSFC in albuterol arm at 12 months (Abstract #P75, World Congress of MS, 2008)  
**Funding:** NIH, NIAID, Autoimmunity Centers of Excellence  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00039988>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) + induction therapy with mitoxantrone for injection concentrate **COMPLETED**  
**Purpose of study:** To evaluate safety and effectiveness of induction with mitoxantrone  
**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (mitoxantrone)  
**Study description:** Randomized, two-arm, open label  
**Dose/route:** Mitoxantrone 12 mg/m<sup>2</sup>/mo iv for 2.5 mos followed by washout, then Copaxone 20 mg/d sc for 12.5 mos vs. Copaxone 20 mg/d sc for 15 mos  
**Outcome parameters:** Frequency of relapse, scoring technique, MRI, quality of life  
**Type of MS:** RR, PR  
**Number of Subjects:** 40  
**Start date:** April 2003  
**Observation period:** 15 months  
**Investigators:** T. Vollmer and others  
**Sites:** Multicenter, United States  
**Results/Publications:** Well tolerated; induction therapy produced 89% greater reduction in Gd lesions at months 6 and 9 and 70% greater reduction at months 12 and 15; results sustained at 36 months; induction therapy resulted in lower proportion of black holes (*Multiple Sclerosis* 2008 Jun;14(5):663-70; Abstract #P3, World Congress of MS 2008)  
**Funding:** Teva Neuroscience  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00203073>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) + induction therapy with mitoxantrone for injection concentrate

**Purpose of study:** To evaluate safety and effectiveness of induction with mitoxantrone

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (mitoxantrone)

**Study description:** Randomized, controlled, examining-MD blinded

**Dose/route:** Mitoxantrone 12 mg/m<sup>2</sup>/mo iv for 3 mos and 6mg/m<sup>2</sup> quarterly for two further pulses + Copaxone 20 mg/d sc

**Outcome parameters:** MSIS, EDSS, relapse rate

**Type of MS:** RR

**Number of Subjects:** 77

**Start date:** April 2005

**Observation period:** 36 months

**Investigators:** M. Boggild and J. Ramtahal

**Sites:** The Walton Centre for Neurology and Neurosurgery, Liverpool, UK and others, UK

**Results/Publications:** 1 case of therapy-related leukemia; relapse rate fell from 1.85 to 0.16; EDSS improved or stable in 69/70 still on Copaxone (Abstract #P498, World Congress of MS, 2008)

**Funding:** National Health Service

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) + prednisone

**Purpose of study:** To control disease course and development of brain lesions, also known as ASSERT Study

**Possible mechanism:** Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)/Closes damaged blood-brain barrier and reduces inflammation in CNS (prednisone)

**Study description:** Double blinded, placebo controlled

**Dose/route:** Copaxone 20 mg/d sc + prednisone po vs. Copaxone + PBO po

**Outcome parameters:** Change in brain volume using SIENA MRI technique

**Type of MS:** RR

**Number of Subjects:** 506

**Start date:** January 2005

**Observation period:** 36 months

**Investigators:** Multiple

**Sites:** Multicenter, United States, Canada, Australia

**Results/Publications:** Not available

**Funding:** Teva Neuroscience

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00203047>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Helminth-induced immunomodulation therapy  
**Purpose of study:** To determine safety and effectiveness in reducing disease activity  
**Possible mechanism:** May stimulate protective immune response  
**Study description:** Baseline versus treatment design, radiologists blinded to treatment status  
**Dose/route:** Solution containing the eggs of the helminth, every two weeks po  
**Outcome parameters:** Gd lesions on serial MRI scans, EDSS, MSFC, relapses, gastrointestinal symptoms, immunology  
**Type of MS:** RR  
**Number of Subjects:** 20  
**Start date:** March 2008  
**Observation period:** 7 months  
**Investigators:** J. Fleming  
**Sites:** University of Wisconsin, Madison  
**Results/Publications:** No safety concerns in 5 subjects during 3 months (Abstract #P07.141, AAN 2009)  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00645749>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec) **COMPLETED**  
**Purpose of study:** To follow patients longitudinally who had been part of the CHAMPS study, also known as CHAMPIONS study  
**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells  
**Study description:** Open label, ongoing neurological surveillance study  
**Dose/route:** 30 mcg/wk im  
**Outcome parameters:** Development of clinically definite MS; subsequent course  
**Type of MS:** Individuals in CHAMPS study (RR, first clinical demyelinating event suggestive of MS)  
**Number of Subjects:** 203  
**Start date:** November 2000  
**Observation period:** 10 years  
**Investigators:** R. Kinkel and others  
**Sites:** Cleveland Clinic Foundation and others, United States and Canada  
**Results/Publications:** 40% reduction in conversion to CDMS in patients treated immediately upon diagnosis of CIS versus those that were delayed by a median of 30 months; 91% of patients had EDSS less than 4.0 after 10 years; 80% of patients on Avonex had EDSS less than 3; and relapse rate for patients with up to 10 years of Avonex was 0.25 (*Neurology* 2006 Mar 14;66(5):678-84; Abstract #P06.137, AAN 2009)  
**Funding:** Biogen Idec, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00179478>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec) + glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.)

**Purpose of study:** To test combination on disease course, also known as CombiRx Study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

**Study description:** Double blinded, placebo controlled

**Dose/route:** Avonex 30 mcg/wk im + Copaxone 20 mg/d sc vs. Avonex + PBO sc vs. Copaxone + PBO im

**Outcome parameters:** Annualized relapse rate, EDSS, MSFC, MSQLI, MRI

**Type of MS:** RR

**Number of Subjects:** 1000

**Start date:** Summer 2004

**Observation period:** 36 months

**Investigators:** F. Lublin and others

**Sites:** Mount Sinai Medical Center, New York, and others, North America

**Results/Publications:** Baseline data on 907 participants (Abstract #S21.005, AAN 2009)

**Funding:** NINDS, agents provided by Biogen Idec, Inc. and Teva Neuroscience

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00211887>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** IFN beta-1a (Avonex<sup>®</sup>, Biogen Idec) + methotrexate + IVMP **COMPLETED**

**Purpose of study:** To control breakthrough disease, also known as ACT study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across, and inducing suppressive T cells (Avonex)/Diminishes leukocyte accumulation (methotrexate)/ Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)

**Study description:** Multicenter, randomized, blinded, parallel-group study

**Dose/route:** Avonex 30 mcg/wk im + PBO po weekly vs. Avonex + methotrexate 20 mg/wk po vs. Avonex + PBO + methylprednisolone 1000 mg/d iv for 3 days every 2 mo vs. Avonex + methotrexate + methylprednisolone

**Outcome parameters:** Relapse rate, brain atrophy progression, MSFC, EDSS, MRI

**Type of MS:** RR with breakthrough disease

**Number of Subjects:** 313

**Start date:** June 2003

**Observation period:** 1 year

**Investigators:** J. Cohen and others

**Sites:** Cleveland Clinic Foundation and others, United States

**Results/Publications:** Combinations generally safe and well tolerated; trends seen for some outcomes for IVMP, but no significant benefit for either adjunctive therapy; data suggested IVMP reduced anti-IFN-beta NAB titers (*Neurology*. 2009 Feb 10;72(6):535-41)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00112034>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec) + methylprednisolone **COMPLETED**

**Purpose of study:** To control development of brain lesions and disease relapses, also known as MECOMBIN study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Closes damaged blood-brain barrier, reducing inflammation in CNS (methylprednisolone)

**Study description:** Placebo controlled

**Dose/route:** Methylprednisolone 500 mg/d po + Avonex 30 mcg/wk im vs. PBO po + Avonex

**Outcome parameters:** EDSS

**Type of MS:** RR

**Number of Subjects:** 341

**Start date:** October 2002

**Observation period:** 3 years

**Investigators:** M. Ravnborg and others

**Sites:** Multicenter, Denmark and Norway

**Results/Publications:** 38% percent fewer relapses in combination group, lesion volume remained stable or decreased, improved slightly on EDSS (Abstract #LB3.002, AAN 2009)

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00168766>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec) + mitoxantrone for injection concentrate

**Purpose of study:** To evaluate safety and effect on disease course

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)/Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cyto

**Study description:** Pilot, open label

**Dose/route:** Avonex 30 mcg/wk im + mitoxantrone 20 mg/mo iv for 6 months

**Outcome parameters:** Safety, MRI, disease progression, time to and frequency of relapse

**Type of MS:** Worsening RR

**Number of Subjects:** 10

**Start date:** March 2002

**Observation period:** 18 months

**Investigators:** N. Kachuck

**Sites:** USC Keck School of Medicine, Los Angeles

**Results/Publications:** Not available

**Funding:** Investigator sponsored

**ClinicalTrials.gov Link:** Not available

**Last update:** 2008

\*\*\*\*\*

**Agent:** Interferon beta-1a (Rebif® [fetal bovine serum (FBS)-free/human serum albumin (HSA)-free formulation], EMD Serono and Pfizer Inc.) **COMPLETED**

**Purpose of study:** To test safety and antigenicity

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Open label

**Dose/route:** 44 mcg tiw sc

**Outcome parameters:** Neutralizing antibodies (NAbs) assessment

**Type of MS:** RR

**Number of Subjects:** 230

**Start date:** January 2005

**Observation period:** 96 weeks

**Investigators:** Multiple

**Sites:** Multicenter

**Results/Publications:** The proportion of NAb-positive patients at 96 weeks was 17.4%, representing relative improvements of 36.3% and 18.7%, respectively, versus original formulation Rebif in REGARD (27.3%) and EVIDENCE (21.4%); adverse events (Rebif new formulation versus Rebif EVIDENCE) included: injection-site reactions (30.8% versus 85.8%), flu-like symptoms (71.5% versus 49.0%), depression/suicidal ideation (6.5% versus 22.7%), hepatic disorders (14.2% versus 18.6%), and cytopenia (13.5% versus 13.0%) (*Multiple Sclerosis* 2009 Feb;15(2):219-28)

**Funding:** EMD Serono, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00110396>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Rebif® [FBS-free/HSA-free formulation], EMD Serono and Pfizer Inc.)

**Purpose of study:** To improve quality of life

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Randomized, two-arm, open label

**Dose/route:** 44 mcg tiw vs. 8.8 mcg tiw for 2 weeks, followed by 22 mcg tiw for 2 weeks, followed by 44 mcg tiw

**Outcome parameters:** Quality of Life, tolerability, injection site reactions, depression, fatigue, impact on analgesic use, safety, compliance

**Type of MS:** Relapsing forms

**Number of Subjects:** 180

**Start date:** April 2007

**Observation period:** 12 weeks

**Investigators:** Multiple

**Sites:** Multicenter, United States

**Results/Publications:** Not available

**Funding:** EMD Serono, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00472797>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Interferon beta-1a (Rebif® [FBS-free/HSA-free formulation], EMD Serono and Pfizer Inc.) **COMPLETED**

**Purpose of study:** To improve quality of life

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Randomized, double-blinded, placebo-controlled

**Dose/route:** PBO for 16 wks then Rebif 44 mcg tiw for 24 wks vs. Rebif 44 mcg tiw for 40 wks

**Outcome parameters:** MRI, biomarkers

**Type of MS:** RR

**Number of Subjects:** 180

**Start date:** December 2006

**Observation period:** 40 weeks

**Investigators:** N. De Stefano

**Sites:** Multicenter, Canada and Europe

**Results/Publications:** At week 16, mean number of combined unique active lesions (primary endpoint) was significantly lower in Rebif group than PBO; T2-weighted lesion volume and number of new T2-weighted and new gadolinium-enhancing lesions were also significantly lower (Abstract #P07.145, AAN 2009)

**Funding:** EMD Serono, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00441103>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1a (Rebif®, EMD Serono and Pfizer Inc.) + estroprogestins

**Purpose of study:** To control disease course and development of new lesions

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)/Immunomodulatory (estroprogestins)

**Study description:** Randomized, examining MD-blind

**Dose/route:** Rebif 44 mcg tiw sc vs. Rebif + desogestrel 150 mcg po + etinilestradiol 20 mcg po vs. Rebif + desogestrel 25 mcg + etinilestradiol 40 mcg

**Outcome parameters:** Frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** RR, women

**Number of Subjects:** 180

**Start date:** May 2004

**Observation period:** 24 months

**Investigators:** C. Pozzilli and others

**Sites:** MS Centre, San Andrea Hospital, University “La Sapienza”, Rome, and others

**Results/Publications:** Not available

**Funding:** University “La Sapienza”

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00151801>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Interferon beta-1a (Rebif<sup>®</sup>, EMD Serono and Pfizer Inc.) vs. Glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) **COMPLETED**

**Purpose of study:** To compare effectiveness in controlling disease course, also known as REGARD study

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Rebif)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)

**Study description:** Randomized, examining MD blinded

**Dose/route:** Rebif 44 mcg tiw sc vs. Copaxone 20 mg/d sc

**Outcome parameters:** Time to first relapse

**Type of MS:** RR

**Number of Subjects:** 764

**Start date:** 2004

**Observation period:** 96 weeks

**Investigators:** D. Mikol and others

**Sites:** Multicenter, worldwide

**Results/Publications:** No significant difference in primary outcome measure or adverse events (Abstracts #119,P232B, ECTRIMS 2007; Abstract #S02.006, AAN 2008)

**Funding:** Serono, Inc., Pfizer Inc.

**ClinicalTrials.gov Link:** Not available

**Last update:** 2008

\*\*\*\*\*

**Agent:** Interferon beta-1b (Betaseron<sup>®</sup>, Bayer HealthCare Pharm., Inc.) **COMPLETED**

**Purpose of study:** To delay time to definite MS in patients with CIS, also known as BENEFIT study, and follow for 5 years

**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells

**Study description:** Double blinded, placebo controlled

**Dose/route:** 250 mcg qod sc vs. PBO sc

**Outcome parameters:** Time to definite MS, frequency of relapse, EDSS, MSFC, MRI

**Type of MS:** First clinical demyelinating event suggestive of MS

**Number of Subjects:** 487

**Start date:** January 2002

**Observation period:** 24 months

**Investigators:** Multiple

**Sites:** Multicenter, Europe, Canada, Israel

**Results/Publications:** Development of MS delayed by 363 days in Betaseron group vs. PBO group; at 5-year follow-up, early treatment reduced risk of developing MS by 37% vs. delayed treatment, and relapse rate by 20%; at 3 years reduced risk for progression of disability by 40% (24% at 5 years, not statistically significant) (*Lancet* 2007;370:389-97; Abstract #P02.148, AAN 2008; Abstract #P901, World Congress of MS 2008)

**Funding:** Schering AG

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00185211>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1b (Betaseron<sup>®</sup>, Bayer HealthCare Pharmaceuticals, Inc.)  
**Purpose of study:** To investigate long-term effects, also known as BEST study  
**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells  
**Study description:** Observational study of over 3500 case reports  
**Dose/route:** 250 mcg qod sc  
**Outcome parameters:** Clinical parameters, MSFC, EuroQoL 5-Dimensions  
**Type of MS:** RR  
**Number of Subjects:** 3566  
**Start date:** 2003  
**Observation period:** 5 years  
**Investigators:** L. Kappos and others  
**Sites:** University Hospitals, Basel, Switzerland, and others, worldwide  
**Results/Publications:** By 12/05, 3566 people recruited; 65.5% have continued treatment for 4 years; of these, 83.7% had no disease progression and 55.7% reduction in relapse rate compared with pre-baseline (Abstract #P595, ECTRIMS 2004; Abstract #P694, ECTRIMS 2006; Abstract #P86, World Congress of MS 2008)  
**Funding:** Bayer HealthCare Pharmaceuticals, Inc.  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Interferon beta-1b (Betaseron<sup>®</sup>, Bayer HealthCare Pharmaceuticals, Inc., two doses) vs. glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) **COMPLETED**  
**Purpose of study:** To determine impact on disease course, brain lesions, also known as BEYOND study  
**Possible mechanism:** Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron)/Peptide copolymer synthesized to mimic myelin basic protein, induces shift from Th1 to Th2 (Copaxone)  
**Study description:** Examining MD blind  
**Dose/route:** Betaseron 250 mcg qod sc vs. 500 mcg qod sc vs. Copaxone 20 mg/d sc  
**Outcome parameters:** Frequency of relapse, scoring technique, MRI  
**Type of MS:** RR  
**Number of Subjects:** 2000  
**Start date:** December 2003  
**Observation period:** 2 years  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** No differences in risk of relapse or MRI findings, indicating that currently approved dose of 250 mcg of Betaseron is optimal dose; no differences in relapse rate or EDSS, but increase in T2 lesions greater among glatiramer group (Abstract #P182, ECTRIMS 2003; Abstract #P06.086, AAN 2004; Abstract #LBS.004, AAN 2008)  
**Funding:** Bayer HealthCare Pharmaceuticals, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00099502>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Interferon tau  
**Purpose of study:** To test safety  
**Possible mechanism:** Promotes shift from Th1 to Th2  
**Study description:** Open label  
**Dose/route:** 3 mg tid po  
**Outcome parameters:** Safety, effectiveness  
**Type of MS:** RR  
**Number of Subjects:** 25  
**Start date:** May 2004  
**Observation period:** 15 months  
**Investigators:** G. Buckle and others  
**Sites:** Brigham and Women's Hospital, Boston, and others  
**Results/Publications:** Significant reduction in mean number of new Gd lesions compared to baseline; 5 people experience relapse on treatment; adverse events generally mild and no one discontinued study drug (Abstract #P451, World Congress of MS 2008)  
**Funding:** Peppen Corporation  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Lamotrigine (Lamictal<sup>®</sup>, GlaxoSmith Kline)  
**Purpose of study:** To control disease course and prevent nervous system damage  
**Possible mechanism:** Anticonvulsant, with possible impact on nerve impulse conduction  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Up to 400 mg/d po vs. PBO po  
**Outcome parameters:** MRI, EDSS, MSFC  
**Type of MS:** SP  
**Number of Subjects:** 120  
**Start date:** January 2006  
**Observation period:** 24 months  
**Investigators:** R. Kapoor and others  
**Sites:** Institute of Neurology, National Hospital for Neurology and Neurosurgery and the Royal Free Hospital, London, UK  
**Results/Publications:** Rationale and design described (Abstract #P794, ECTRIMS 2006)  
**Funding:** MS Society of Great Britain and Northern Ireland  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00257855>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Laquinimod **COMPLETED**  
**Purpose of study:** To control disease course and development of brain lesions  
**Possible mechanism:** Immunomodulatory  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 0.3 mg/d po vs. 0.6 mg/d po vs. PBO po  
**Outcome parameters:** MRI, relapse rate  
**Type of MS:** RR  
**Number of Subjects:** 306  
**Start date:** March 2005  
**Observation period:** 36 weeks  
**Investigators:** G. Comi and others  
**Sites:** Multiple  
**Results/Publications:** Cumulative number of active lesions reduced by 40.4% in .6 mg group compared with PBO; no benefit in .3 mg group; increases in liver enzymes in 23.4% of the .6 mg group, 33% of the .3 mg group, and 10.8% of PBO group; 1 patient in .6 mg group developed Budd-Chiari syndrome (liver disease) after 1 month on treatment (*Lancet*. 2008 Jun 21;371(9630):2085-92.)  
**Funding:** Teva Neuroscience  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00349193>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Laquinimod  
**Purpose of study:** To control disease course and development of brain lesions, also known as ALLEGRO study  
**Possible mechanism:** Immunomodulatory  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 0.6 mg/d po vs. PBO po  
**Outcome parameters:** Frequency of relapse  
**Type of MS:** RR  
**Number of Subjects:** 1000  
**Start date:** December 2007  
**Observation period:** 2 years  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** Teva Neuroscience  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00509145>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Laquinimod vs. interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)  
**Purpose of study:** To control disease course and development of brain lesions, also known as BRAVO study  
**Possible mechanism:** Immunomodulatory (laquinimod)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)  
**Study description:** Randomized, blinded, placebo controlled  
**Dose/route:** 0.6 mg/d po vs. PBO po vs. Avonex 30 mcg/wk im  
**Outcome parameters:** Frequency of relapse  
**Type of MS:** RR  
**Number of Subjects:** 1200  
**Start date:** April 2008  
**Observation period:** 24 months  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** Teva Neuroscience  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00605215>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** MBP8298 (dirucotide)  
**Purpose of study:** To control disease activity and test safety, also known as MAESTRO-01  
**Possible mechanism:** Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** MBP8298 500 mg iv every 6 mos vs. PBO iv  
**Outcome parameters:** EDSS, MSFC, relapse rates, MSQOL-54  
**Type of MS:** SP  
**Number of Subjects:** 550  
**Start date:** December 2004  
**Observation period:** 24 months  
**Investigators:** M. Freedman and others  
**Sites:** University of Alberta and others, Canada and Europe  
**Results/Publications:** Rationale and design described (Abstract #P01.084, AAN 2006)  
**Funding:** BioMS Medical Corp.  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** MBP8298 (dirucotide)  
**Purpose of study:** To control disease activity and test safety, also known as MAESTRO-03  
**Possible mechanism:** Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** MBP8298 500 mg iv every 6 mos vs. PBO iv  
**Outcome parameters:** EDSS  
**Type of MS:** SP  
**Number of Subjects:** 510  
**Start date:** June 2007  
**Observation period:** 24 months  
**Investigators:** C. Markowitz and others  
**Sites:** MS Center of the University of Pennsylvania, Philadelphia, and others, United States  
**Results/Publications:** Not available  
**Funding:** BioMS Medical Corp.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00468611>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** MBP8298 (dirucotide) **COMPLETED**  
**Purpose of study:** To control disease activity and test safety, also known as MINDSET-01  
**Possible mechanism:** Synthetic myelin basic protein peptide; induces immunological tolerance against a specific epitope of myelin  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** MBP8298 500 mg iv; 5 single doses at baseline, and months 3,9,15,21  
**Outcome parameters:** Frequency of relapse, scoring technique  
**Type of MS:** RR  
**Number of Subjects:** 215  
**Start date:** November 2006  
**Observation period:** 15 months  
**Investigators:** Multiple  
**Sites:** Multiple, Europe  
**Results/Publications:** Did not reduce relapse rate significantly (primary outcome) and did not significantly impact MRI activity; significantly reduced disease progression as measured by mean change in EDSS and MSFC (secondary endpoints) (BioMS Medical press release, January 30, 2009)  
**Funding:** BioMS Medical Corp.  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Memantine (Namenda<sup>®</sup>, Forest Pharmaceuticals)

**COMPLETED**

**Purpose of study:** To improve cognitive function

**Possible mechanism:** Blocks NMDA receptors

**Study description:** Double blinded, placebo controlled

**Dose/route:** 5 mg/d po increased in 5-mg increments to 20 mg/d over 4 wks vs. PBO po

**Outcome parameters:** PASAT, California Verbal Learning Test II, additional neuropsychological tests and questionnaires

**Type of MS:** All types

**Number of Subjects:** 126

**Start date:** April 2004

**Observation period:** 16 weeks

**Investigators:** D. Bourdette and others

**Sites:** Oregon Health & Science University, Portland, and others, United States

**Results/Publications:** Memantine safe and well tolerated but showed no significant effectiveness as measured by PASAT and CVLT-II (Abstract #S11.002, AAN 2009)

**Funding:** Forest Laboratories, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00300716>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Methylprednisolone

**Purpose of study:** To compare oral versus intravenous delivery to control development of brain lesions and treat disease relapses, also known as OMEGA study

**Possible mechanism:** Closes damaged blood-brain barrier, reducing inflammation in CNS

**Study description:** Double blinded, placebo controlled

**Dose/route:** 1000 mg iv vs. 1400 mg/d po, for 5 days

**Outcome parameters:** EDSS, MSFC, frequency of relapse, Targeted Neurological Deficit

**Type of MS:** Relapse in past 7 days

**Number of Subjects:** 140

**Start date:** October 2002

**Observation period:** 1 year

**Investigators:** T. DeAngelis and others

**Sites:** Mount Sinai Medical Center, and others in New York, NY

**Results/Publications:** Not available

**Funding:** National MS Society

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00418145>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Minocycline  
**Purpose of study:** To control development of brain lesions  
**Possible mechanism:** Inhibits matrix metalloproteinases  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Minocycline 100 mg bid po vs. PBO po  
**Outcome parameters:** MS defined by McDonald Criteria  
**Type of MS:** CIS  
**Number of Subjects:** 100  
**Start date:** April 2008  
**Observation period:** 2 years  
**Investigators:** L. Metz and others  
**Sites:** Multiple, Canada  
**Results/Publications:** Not available  
**Funding:** MS Society of Canada  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00666887>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Minocycline + Interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)  
**Purpose of study:** To control development of brain lesions  
**Possible mechanism:** Inhibits matrix metalloproteinases (minocycline)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)  
**Study description:** Open label  
**Dose/route:** Avonex 30 mcg/wk im + minocycline 100 mg bid po  
**Outcome parameters:** Frequency of relapse, EDSS, MSFC, MRI  
**Type of MS:** RR  
**Number of Subjects:** 20  
**Start date:** June 2003  
**Observation period:** 15 months  
**Investigators:** R. Bashir, D. Kirby  
**Sites:** Creighton University, Bellevue, NE  
**Results/Publications:** 11 patients completed 1 year on study and 2 patients dropped out (reversible hair loss, depression); side effects included vaginal candidiasis, nausea, dizziness, headache, depression; 6 patients had increased hepatic enzymes (minimal and transient in four, two requiring Avonex dose adjustment); none of 5 patients completing the study so far had enhancing brain lesions on MRI (Abstract #S03, CMSC 2005)  
**Funding:** Biogen Idec, Inc.  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate  
**Purpose of study:** To evaluate long-term safety, also known as RENEW study  
**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion  
**Study description:** Registry to evaluate open-label therapy  
**Dose/route:** 12 mg/m<sup>2</sup> iv every 3 mos up to a cumulative dose of 140 mg/m<sup>2</sup>  
**Outcome parameters:** Adverse events, left ventricular ejection fraction, relapse rate  
**Type of MS:** Worsening RR, and SP  
**Number of Subjects:** 500  
**Start date:** February 2001  
**Observation period:** 5 years  
**Investigators:** Multiple  
**Sites:** Multicenter  
**Results/Publications:** Mean duration of treatment, 1.5 years; mean cumulative dose per patient, 69.7 m/m<sup>2</sup>; 343 relapses reported in 247 patients (median time to first relapse, 160 days); 405 post-baseline LVEF tests performed on 200 patients, 25 patients showed LVEF <50%; 8 cases of cardiac heart failure; 2 cases of therapy-related leukemia (Abstract #P500, World Congress of MS 2008)  
**Funding:** EMD Serono Inc.  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate **COMPLETED**  
**Purpose of study:** To assess quality of life and cost of disease in people with MS treated with mitoxantrone in RENEW study  
**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion  
**Study description:** Prospective study  
**Dose/route:** 12 mg/m<sup>2</sup> iv every 3 mos up to a cumulative dose of 140 mg/m<sup>2</sup>  
**Outcome parameters:** Health Survey (SF-12 v2), Health Utilities Index, Patient Determined Disease Steps  
**Type of MS:** RR, SP  
**Number of Subjects:** 113  
**Start date:** Based on enrollment in RENEW study  
**Observation period:** 5 years  
**Investigators:** T. Vollmer  
**Sites:** Barrow Neurological Institute, St. Joseph's Hospital, Phoenix, AZ  
**Results/Publications:** 113 (44%) of 500 RENEW patients completed both baseline and closing questionnaires; patients demonstrated stability in 8/11 performance scale domains and QOL over a mean of 35 months after enrollment in RENEW; Patient-Determined Disease Step, mobility, and bladder/bowel subscores worsened significantly; fatigue improved significantly (Abstract #P06, CMSC 2006)  
**Funding:** EMD Serono, Inc.  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate  
**Purpose of study:** To determine long-term safety  
**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion  
**Study description:** Annual assessment of safety profile  
**Dose/route:** Monthly for 6 mos vs. every 3 mos; median cumulative dose, 73 mg/m<sup>2</sup>  
**Outcome parameters:** Safety profile  
**Type of MS:** RR, SP, PP  
**Number of Subjects:** 802  
**Start date:** 2000  
**Observation period:** 5 years  
**Investigators:** G. Edan and others  
**Sites:** CHU de Rennes, France, and others  
**Results/Publications:** Follow-up of 5361 patient-years; 1 case of acute congestive heart failure; 39 patients experienced at least one asymptomatic LVEF reduction under 50%; persisted in 10 patients; 2 cases of therapy-related leukemia (1 death and 1 remission); 17.3% of 317 women treated before age 45 developed persistent amenorrhea (Abstract #P06.93, AAN 2004; Abstract #S02.006, AAN 2006; Abstract #P738, ECTRIMS 2006)  
**Funding:** Not available  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate **TERMINATED**  
**Purpose of study:** To evaluate safety and to control disease course  
**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion  
**Study description:** Randomized, double blinded, three arms  
**Dose/route:** 5 mg/m<sup>2</sup> iv vs. 9 mg/m<sup>2</sup> vs. 12 mg/m<sup>2</sup> every 3 mos up to 24 mos  
**Outcome parameters:** EDSS, change of ambulation index, time to first relapse requiring corticoid treatment, MRI  
**Type of MS:** SP  
**Number of Subjects:** 336  
**Start date:** March 2005  
**Observation period:** 5 years  
**Investigators:** Multiple  
**Sites:** Multicenter, Germany  
**Results/Publications:** Terminated due to poor patient recruitment (communication with sponsor)  
**Funding:** Wyeth Pharma GmbH, Germany  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00146159>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec) or glatiramer acetate (Copaxone<sup>®</sup>, Teva Pharmaceutical Industries Ltd.) **COMPLETED**

**Purpose of study:** To evaluate safety and to control disease course

**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (mitoxantrone)/ Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Open label

**Dose/route:** Mitoxantrone 12 mg/m<sup>2</sup> every 3 mos (4 times) + Avonex 30 mcg/wk im vs. mitoxantrone + Copaxone 20 mg/d sc

**Outcome parameters:** Safety, scoring technique, MRI

**Type of MS:** RR, SP

**Number of Subjects:** 50

**Start date:** September 2001

**Observation period:** 12 months

**Investigators:** P. Calabresi and others

**Sites:** University of Maryland, Baltimore, and others

**Results/Publications:** No difference between groups; approximately 25% of patients had reduction in left ventricular ejection fraction of 10% or greater after 4 doses of mitoxantrone (Abstract #S12.006, AAN 2004)

**Funding:** Serono Inc.

**ClinicalTrials.gov Link:** Not available

**Last update:** 2008

\*\*\*\*\*

**Agent:** Mitoxantrone for injection concentrate + interferon beta-1b (Betaseron<sup>®</sup>, Bayer HealthCare Pharmaceuticals, Inc.) **TERMINATED**

**Purpose of study:** To control disease course using pretreatment with mitoxantrone

**Possible mechanism:** Inhibits B cell, T cell, and macrophage proliferation, antigen presentation and inflammatory cytokine secretion (mitoxantrone)/ Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Betaseron)

**Study description:** Physician blinding

**Dose/route:** Mitoxantrone 20 mg/m<sup>2</sup> iv + methylprednisolone 20 mg (6 mos), then Betaseron 250 mcg qod sc vs. methylprednisolone + Betaseron (6 mos), then all Betaseron

**Outcome parameters:** Frequency of relapse, EDSS, MRI

**Type of MS:** RR

**Number of Subjects:** 220

**Start date:** January 1999

**Observation period:** 3 years

**Investigators:** G. Edan

**Sites:** Multicenter, France and Italy

**Results/Publications:** Terminated (ClinicalTrials.gov listing #NCT00219908)

**Funding:** French Health Ministry, Schering AG

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00219908>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** MN-166

**COMPLETED**

**Purpose of study:** To test safety and control disease course

**Possible mechanism:** Inhibits leukotriene activity, phosphodiesterases and nitric oxide synthase; may be neuroprotective

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** MN-166 20 mg tid po vs. MN-166 10 mg tid vs. PBO po

**Outcome parameters:** MRI, frequency of relapse, EDSS

**Type of MS:** RR, SP

**Number of Subjects:** 300

**Start date:** July 2005

**Observation period:** 24 months

**Investigators:** Multiple

**Sites:** Multicenter, Eastern Europe

**Results/Publications:** No significant reduction of cumulative active lesions, primary endpoint; significant reduction in EDSS progression and black holes; gastrointestinal events more common in MN-166 groups and depression more common in higher-dose group in year 2 (Abstract #52, ECTRIMS 2007; Abstract #P48, World Congress of MS 2008)

**Funding:** MediciNova, Inc.

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Mycophenolate mofetil (CellCept<sup>®</sup>, Roche Laboratories, Inc.) + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)

**Purpose of study:** To test safety and tolerability

**Possible mechanism:** Inhibits proliferation of T/B cells, suppresses antibody formation (CellCept)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** Avonex 30 mcg/wk im + CellCept 250-1000 mg bid po vs. Avonex + PBO

**Outcome parameters:** MRI, EDSS, quality of life, frequency of relapse, pharmacogenomics

**Type of MS:** RR

**Number of Subjects:** 24

**Start date:** July 2004

**Observation period:** 12 months

**Investigators:** E. Frohman

**Sites:** University of Texas Southwestern Medical Center at Dallas

**Results/Publications:** Not available

**Funding:** Biogen Idec, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00223301>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Mycophenolate mofetil (CellCept<sup>®</sup>, Roche Laboratories, Inc.) + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)

**Purpose of study:** To test safety and tolerability

**Possible mechanism:** Inhibits proliferation of T and B cells, suppresses antibody formation (CellCept)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)

**Study description:** Randomized, open label, parallel group

**Dose/route:** Avonex 30 mcg/wk or CellCept 500-1000 mg bid po for 6 mos; then Avonex 30 mcg/wk im + CellCept 500-1000 mg bid po for 6 mos

**Outcome parameters:** EDSS, MSFC, frequency of relapse, MRI

**Type of MS:** RR

**Number of Subjects:** 60

**Start date:** 2006

**Observation period:** 3 years

**Investigators:** E. Frohman and others

**Sites:** University of Texas Southwestern Medical Center at Dallas, and others, United States

**Results/Publications:** During first 6 mos, no difference between CellCept and Avonex on primary MRI endpoints; CellCept group showed 45%-60% lower accumulation of Gd, T2 and combined active lesions compared to Avonex, but not significant; combination showed slight benefit on accumulation of Gd, T2 and combined active lesions in original Avonex group, but not CellCept group; safe, well tolerated (Abstract #P02.175, AAN 2008)

**Funding:** Aspreva Pharmaceuticals

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00324506>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Low dose naltrexone

**COMPLETED**

**Purpose of study:** To test safety and efficacy on spasticity, pain, fatigue and depression

**Possible mechanism:** Semi-synthetic opiate antagonist

**Study description:** Pilot, open label

**Dose/route:** 5 mg/d po

**Outcome parameters:** Fatigue Severity Scale, Visual Analogue Scale, Ashworth modified scale, Beck depression scale

**Type of MS:** PP

**Number of Subjects:** 40

**Start date:** November 2006

**Observation period:** 6 months

**Investigators:** Multiple

**Sites:** San Raffaele Scientific Institute, and others, Italy

**Results/Publications:** 35 patients completed the trial; well tolerated; statistically significant reduction in spasticity (*Multiple Sclerosis* 2008 Sep;14(8):1076-83)

**Funding:** Italian MS Foundation

**ClinicalTrials.gov Link:** Not available

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Natalizumab (Tysabri<sup>®</sup>, Biogen Idec and Elan)  
**Purpose of study:** Evaluation of Natalizumab for thE Relief of MS Associated FatiGue, also known as ENER-G study  
**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin  
**Study description:** Open label  
**Dose/route:** Tysabri 300 mg every 4 wks iv  
**Outcome parameters:** Visual Analog Scale for fatigue, Modified Fatigue Impact Scale, Fatigue Severity Scale, Automated Neuropsychology Assessment Metrics  
**Type of MS:** Relapsing forms  
**Number of Subjects:** 200  
**Start date:** September 2007  
**Observation period:** 12 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** Biogen Idec, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00464074>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Natalizumab (Tysabri<sup>®</sup>, Biogen Idec and Elan)  
**Purpose of study:** To determine effects of treatment on vaccination response  
**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin  
**Study description:** Randomized, open label  
**Dose/route:** Tysabri 300 mg iv every 4 weeks for at least 9 mos, along with 3 immunizations of keyhole limpet hemocyanin sc at Day 168, 182, 196 and immunization of tetanus diphtheria vaccine im at Day 168 vs. 3 immunizations of keyhole limpet hemocyanin sc at Day 0,  
**Outcome parameters:** Effect of Tysabri on antibody response and circulating lymphocyte subsets (CD3+, CD4+, CD8+, CD19+ and CD56+) over time, and assessment of alpha-4 saturation and alpha-4 expression at specified time points  
**Type of MS:** Relapsing forms  
**Number of Subjects:** 46  
**Start date:** November 2007  
**Observation period:** 8 months  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** Biogen Idec  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00536120>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Natalizumab (Tysabri<sup>®</sup>, Biogen Idec and Elan)  
**Purpose of study:** To determine effects on MS-related fatigue  
**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin  
**Study description:** Open label  
**Dose/route:** Tysabri 300 mg every 4 wks iv  
**Outcome parameters:** Fatigue Severity Scale; Modified Fatigue Impact Scale  
**Type of MS:** RR  
**Number of Subjects:** 50  
**Start date:** Ongoing  
**Observation period:** 6 months  
**Investigators:** N. Putzki and others  
**Sites:** University Clinic Essen, Germany  
**Results/Publications:** Interim analysis showed positive effect of natalizumab on fatigue (Abstract #P02.178, AAN 2008)  
**Funding:** Biogen Idec  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Natalizumab (Tysabri<sup>®</sup>, Biogen Idec and Elan)  
**Purpose of study:** Tysabri Global Observational Program In Safety, also known as TYGRIS  
**Possible mechanism:** Interferes with movement of immune cells across the blood-brain barrier by attaching to alpha 4-integrin  
**Study description:** Open label, observational cohort  
**Dose/route:** 300 mg every 4 wks iv  
**Outcome parameters:** Long-term safety data  
**Type of MS:** Relapsing forms  
**Number of Subjects:** 2500  
**Start date:** January 2007  
**Observation period:** 5 years  
**Investigators:** Multiple  
**Sites:** Multicenter, United States and Canada  
**Results/Publications:** 5111 patients enrolled; serious adverse event incidence was 4%, most frequently hypersensitivity reactions and infections; 2 cases of PML in Tygris population (6 post-marketing cases overall as of 5/8/09) (Abstract #S11.005, AAN 2009)  
**Funding:** Biogen Idec  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00477113>  
**Last update:** 2009

\*\*\*\*\*

**Agent:** Nerispiridine  
**Purpose of study:** To evaluate effects on visual function  
**Possible mechanism:** Sodium/potassium channel blocker  
**Study description:** Randomized, double blinded, placebo controlled, crossover  
**Dose/route:** Nerispiridine 50 mg/d po vs. 400 mg/d po vs. PBO  
**Outcome parameters:** Visual evoked potential  
**Type of MS:** All types, with history of optic neuritis  
**Number of Subjects:** 30  
**Start date:** November 2008  
**Observation period:** 5 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** sanofi-aventis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00772525>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Ocrelizumab vs. interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)  
**Purpose of study:** To evaluate safety and effectiveness in reducing disease activity  
**Possible mechanism:** Binds to CD20 antigen on B cells and induces B-cell lysis (ocrelizumab)/ Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)  
**Study description:** Randomized, parallel-group, partially blinded  
**Dose/route:** Ocrelizumab 1000 mg iv vs. 300 mg iv vs. PBO IV vs. Avonex 30 mcg/wk im  
**Outcome parameters:** MRI  
**Type of MS:** RR  
**Number of Subjects:** 200  
**Start date:** June 2008  
**Observation period:** 3 years  
**Investigators:** Multiple  
**Sites:** Multicenter, United States  
**Results/Publications:** Not available  
**Funding:** Genentech, Inc., F. Hoffman-Laroche Ltd.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00676715>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** PI-2301 (co-polymer)  
**Purpose of study:** To evaluate safety, tolerability, and pharmacokinetics  
**Possible mechanism:** Immunomodulation via the MHC Class II receptor  
**Study description:** Randomized, double blinded, placebo controlled, multiple doses  
**Dose/route:** PI-2301/wk sc (4 doses) vs PBO/wk sc for 8 wks; then open label for 4 wks  
**Outcome parameters:** Safety, tolerability, MRI, EDSS, immunological markers  
**Type of MS:** SP  
**Number of Subjects:** 0  
**Start date:** May 2008  
**Observation period:** 14 weeks  
**Investigators:** G. Edan and others  
**Sites:** Multiple, France  
**Results/Publications:** Not available  
**Funding:** Peptimmune  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Pixantrone (BBR 2778)  
**Purpose of study:** To test safety, control development of brain lesions and determine impact on immune function, also known as PIXAMS study  
**Possible mechanism:** Intercalates DNA, inhibits topoisomerase II, cytotoxic  
**Study description:** Open label  
**Dose/route:** Pixantrone 120 mg/m<sup>2</sup> iv every 3 wks for 12 wks  
**Outcome parameters:** Immunosuppressive effects, Gd+ lesion evolution, safety  
**Type of MS:** Aggressive RR or SP MS  
**Number of Subjects:** 20  
**Start date:** Fall 2008  
**Observation period:** 2 years  
**Investigators:** R. Gonsette and others  
**Sites:** Belgium National Centre for Multiple Sclerosis, Melsbroek, Belgium, and others, Europe  
**Results/Publications:** Not available  
**Funding:** Fondation-Charcot-Stichting, Belgium  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Plasmapheresis (plasma exchange) **COMPLETED**  
**Purpose of study:** To assess the effect of plasma exchange in accelerating the clearance of natalizumab  
**Possible mechanism:** Removes circulating antibodies from blood, including antibody-based therapies such as natalizumab  
**Study description:** Open label  
**Dose/route:** Plasma exchange qod iv, three times over 5 days (Group 1: Monday-Thursday-Monday; Group 2: Monday-Wednesday-Friday)  
**Outcome parameters:** Natalizumab concentration; VLA-4 receptor saturation; leukocyte migration across a synthetic blood-brain barrier  
**Type of MS:** RR  
**Number of Subjects:** 12  
**Start date:** May 2007  
**Observation period:** 24 weeks  
**Investigators:** R. Fox; B. Khatri; G. Giovannoni  
**Sites:** Mellen Center, Cleveland Clinic, Cleveland, OH; St. Luke's Medical Center of Aurora Health Care, Milwaukee, WI  
**Results/Publications:** One week after the final session, Tysabri concentration decreased by average of 92% compared with levels before plasma exchange (*Neurology* 2009 Feb 3;72(5):402-9)  
**Funding:** Biogen Idec, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00424788>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Pravastatin (Pravachol<sup>®</sup>, Bristol-Myers Squibb) **COMPLETED**  
**Purpose of study:** To test tolerability and effectiveness in controlling disease course  
**Possible mechanism:** Promotes anti-inflammatory Th2 response  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** 40 mg/d po vs. PBO po  
**Outcome parameters:** MRI, MSFC  
**Type of MS:** RR  
**Number of Subjects:** 40  
**Start date:** November 2005  
**Observation period:** 6 months  
**Investigators:** D. Laplaud and others  
**Sites:** University Hospital, Nantes, France  
**Results/Publications:** Gd lesions reduced by 85% at month 6 in pravastatin group vs. 44% in PBO group; viral infections most frequent adverse event, recorded with same frequency in both groups (Abstract #P457, World Congress of MS 2008)  
**Funding:** Public Funds  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00200655>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Pregabalin (Lyrica<sup>®</sup>, Pfizer, Inc.) vs. paroxetine (Paxil<sup>®</sup>, GlaxoSmith Kline)  
**Purpose of study:** To improve MS-related pain  
**Possible mechanism:** GABA analogue, thought to act as Ca<sup>++</sup> channel modulator, decreasing Ca<sup>++</sup> influx into nerve cells, affecting release of pain neurotransmitters (Lyrica)/selective serotonin reuptake inhibitor (Paxil)  
**Study description:** Randomized, open label  
**Dose/route:** Paroxetine 50 mg/d po vs. pregabalin 600 mg bid po  
**Outcome parameters:** Visual Analog Scale pain score, quality of life  
**Type of MS:** All types, with neuropathic pain  
**Number of Subjects:** 80  
**Start date:** March 2006  
**Observation period:** 8 weeks  
**Investigators:** M. Melanson, M. Namaka, D. Turcotte  
**Sites:** MS Clinic, Health Sciences Centre, Winnipeg, Manitoba, Canada  
**Results/Publications:** Not available  
**Funding:** Not available  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00291148>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Progesterone + estradiol  
**Purpose of study:** To prevent postpartum MS relapses, also known as POPARTMUS study  
**Possible mechanism:** Promotes anti-inflammatory Th2 response  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** Progesterone 10 mg/d po + estgradiol 75 mcg/wk pc vs. PBO po + PBO pc  
**Outcome parameters:** Rate of relapse 12 wks after delivery  
**Type of MS:** Relapsing, women  
**Number of Subjects:** 300  
**Start date:** June 2005  
**Observation period:** 6 months  
**Investigators:** C. Confavreux and others  
**Sites:** Hospices Civils de Lyon, and others, Europe  
**Results/Publications:** Not available  
**Funding:** French Ministry of Health, The Myelin Project, European Leukodystrophy Association, Association pour la Recherche sur la Sclérose en Plaques  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00127075>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Rehabilitation  
**Purpose of study:** To determine whether exercise can improve depression  
**Possible mechanism:** Effects on brain dopamine, noradrenaline and serotonin transmission  
**Study description:** Trained examiner blinded  
**Dose/route:** Home exercise program, motivational interview and telephone follow-up vs. delayed treatment  
**Outcome parameters:** Structured Clinical Interview for DSM-III-R, Hamilton Depression Rating Scale, Hopkins Symptom Checklist  
**Type of MS:** All types  
**Number of Subjects:** 108  
**Start date:** February 2005  
**Observation period:** 6 months  
**Investigators:** C. Bombardier and others  
**Sites:** University of Washington MS Rehabilitation Research & Training Center  
**Results/Publications:** Not available  
**Funding:** National Institute on Disability and Rehabilitation Research  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Rehabilitation  
**Purpose of study:** To improve function and participation  
**Possible mechanism:** Improves physical function, decreases pain, and improves participation in life activities  
**Study description:** Trained examiner blinded  
**Dose/route:** Motivational interview, physical therapy, and home exercise program with telephone follow-up vs. no treatment  
**Outcome parameters:** MSFC, Ashworth Spasticity Index, Brief Pain Inventory, Community Integration Questionnaire  
**Type of MS:** All types  
**Number of Subjects:** 120  
**Start date:** June 2004  
**Observation period:** Until September 2008  
**Investigators:** J. Bowen and others  
**Sites:** University of Washington MS Rehabilitation Research & Training Center  
**Results/Publications:** Not available  
**Funding:** National Institute on Disability and Rehabilitation Research  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Rehabilitation (memory retraining)  
**Purpose of study:** To improve new learning and memory  
**Possible mechanism:** Engages additional cortical regions in encoding new information into long-term memory  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Memory retraining protocol comprising 10 sessions vs. control protocol comprising 10 sessions  
**Outcome parameters:** Memory tests; reports of emotional functioning, memory functioning, and quality of life  
**Type of MS:** RR, progressive  
**Number of Subjects:** 200  
**Start date:** February 2005  
**Observation period:** 8 months  
**Investigators:** N. Chiaravalloti  
**Sites:** Kessler Medical Rehabilitation Research and Education Center, West Orange, NJ  
**Results/Publications:** Not available  
**Funding:** National Institutes of Health  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00166283>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Rehabilitation (robotic locomotor training)  
**Purpose of study:** To improve walking ability  
**Possible mechanism:** May help restore strength, balance, recognition of sensory cues and other factors that make walking possible  
**Study description:** Treadmill training using a robot vs. non-treadmill exercise program  
**Dose/route:** Treadmill training using a robot vs. non-treadmill exercise program three times weekly for 12 wks  
**Outcome parameters:** Overground walking speed, performance on 6-minute walk  
**Type of MS:** PP, SP  
**Number of Subjects:** 40  
**Start date:** April 2006  
**Observation period:** 12 weeks  
**Investigators:** B. Giesser  
**Sites:** The Marilyn Hilton MS Achievement Center at UCLA  
**Results/Publications:** Preliminary data suggest a potentially beneficial effect on cognitive performance (Abstract #P08.165, AAN 2009)  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00607126>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Repetitive Transcranial Magnetic Stimulation (rTMS) **COMPLETED**  
**Purpose of study:** To improve walking ability  
**Possible mechanism:** Modulation of spinal inhibitory interneurons, by TMS-induced activation of corticospinal projections  
**Study description:** Open label  
**Dose/route:** 10Hz rTMS, 10 trains of 100 stimuli (1000 total stimuli) daily, for 10 consecutive days  
**Outcome parameters:** EDSS, Modified Ashworth Scale  
**Type of MS:** RR  
**Number of Subjects:** 5  
**Start date:** October 2007  
**Observation period:** 25 days  
**Investigators:** S. Deftereos, G. Panagopoulos, C. Karageorgiou  
**Sites:** Neurology Department, Athens General Hospital “G. Gennimatas”, Athens, Greece  
**Results/Publications:** Median EDSS was 5.5 (range 5 – 6) before treatment and 5 (4.5 – 5) after treatment; median reduction in EDSS was 0.5 (0.5 – 1); median Modified Ashworth Scale was 3 (2-3) before treatment and 2 (1-2) after treatment; effects still present at 2-week follow up (Abstract #P02.159, AAN 2008)  
**Funding:** Not available  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008

\*\*\*\*\*

**Agent:** RG2077 **COMPLETED**  
**Purpose of study:** To test safety and immune mechanisms  
**Possible mechanism:** Antibody (immunoglobulin) to CTLA4, blocks costimulation  
**Study description:** Open label  
**Dose/route:** Single infusion, 2.0 mg/kg, 10.0 mg/kg, 20.0 mg/kg, or 35.0 mg/kg; and multi-dose of 10 mg/kg iv  
**Outcome parameters:** Safety, immunologic/mechanistic studies, MRI  
**Type of MS:** RR  
**Number of Subjects:** 16  
**Start date:** March 2003  
**Observation period:** 5 months  
**Investigators:** S. Khoury and others  
**Sites:** Harvard Medical School, Boston, and others  
**Results/Publications:** 63 adverse events reported in 16 participants, of which 59 were mild and 4 moderate; 9 patients had new Gd lesions during the study; immunologic analysis showed reduction in MBP proliferation and decreased IFN-gamma production by MBP-specific lines (*Neurology*. 2008 Sep 16;71(12):917-24)  
**Funding:** Immune Tolerance Network  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00076934>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Riluzole (Rilutek<sup>®</sup>, sanofi-aventis) + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec)  
**Purpose of study:** To evaluate neuroprotective ability in MS  
**Possible mechanism:** Inhibits glutamate toxicity to nerve cells (Rilutek)/Slows down immune response, possibly by interfering with T cell activation and movement across blood-brain barrier, and inducing suppressive T cells (Avonex)  
**Study description:** Double blinded, placebo controlled  
**Dose/route:** Rilutek 50 mg/d po vs. PBO po for one month; Avonex 30 mcg/wk im added after 3 mos if liver function normal  
**Outcome parameters:** Frequency and duration of relapse, safety, evoked potentials, MRI  
**Type of MS:** early MS, CIS  
**Number of Subjects:** 40  
**Start date:** July 2006  
**Observation period:** 2 years  
**Investigators:** E. Waubant  
**Sites:** University of California, San Francisco  
**Results/Publications:** 10 patients have completed more than 3 months on combined therapy; a few have reported transient mild dizziness (Abstract #P530, World Congress of MS 2008)  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00501943>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Rituximab (Rituxan<sup>®</sup>, Genentech and Biogen Idec) **COMPLETED**  
**Purpose of study:** To control development of brain lesions  
**Possible mechanism:** Binds to CD20 antigen on B cells and induces B-cell lysis  
**Study description:** Open label, neuroradiologist blinding  
**Dose/route:** 375 mg/m<sup>2</sup> iv (4 times)  
**Outcome parameters:** MRI  
**Type of MS:** RR, not responsive to standard immunomodulatory treatment  
**Number of Subjects:** 26  
**Start date:** March 2002  
**Observation period:** 1 year  
**Investigators:** A. Cross  
**Sites:** Washington University, St. Louis  
**Results/Publications:** At 24 weeks, EDSS unchanged, MSFC improved over baseline (driven by performance on PASAT); treatment depleted T cells as well as B cells (Abstracts #31,P476 World Congress of MS 2008)  
**Funding:** National MS Society  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Rituximab (Rituxan<sup>®</sup>, Genentech and Biogen Idec) **COMPLETED**

**Purpose of study:** To evaluate tolerability, effect on disease activity

**Possible mechanism:** Binds to CD20 antigen on B cells and induces B-cell lysis

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 1 g/d iv (eight times) vs. PBO iv

**Outcome parameters:** Time to confirmed disease progression, MRI

**Type of MS:** PP

**Number of Subjects:** 435

**Start date:** April 2004

**Observation period:** 30 months

**Investigators:** Multiple

**Sites:** Multicenter, United States and Canada

**Results/Publications:** Time to confirmed disease progression at 96 weeks was not significantly different between rituximab and PBO; planned subgroup analysis indicates time to progression was significantly increased in rituximab-treated patients younger than 51 years, those with Gd lesions, and those younger than 51 years with Gd lesions compared with PBO group; serious infections occurred in 4.5% rituximab versus <1.0% of PBO (Abstract #S21.003, AAN 2009)

**Funding:** Genentech, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00087529>

**Last Update:** 2009

\*\*\*\*\*

**Agent:** Rituximab (Rituxan<sup>®</sup>, Genentech and Biogen Idec) **COMPLETED**

**Purpose of study:** To evaluate tolerability, effect on disease activity

**Possible mechanism:** Binds to CD20 antigen on B cells and induces B-cell lysis

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 1 g/d iv (on day 1 and day 15) vs. PBO iv

**Outcome parameters:** Frequency of relapse, scoring technique, MRI

**Type of MS:** RR

**Number of Subjects:** 104

**Start date:** December 2004

**Observation period:** 48 weeks

**Investigators:** Multiple

**Sites:** Multicenter, United States and Canada

**Results/Publications:** 91% reduction in Gd+ lesion count and reduced proportion of patients with relapses vs. PBO; except for infusion-associated events, rates of adverse events comparable; 79 patients completed 48 wks and reduction in number of active lesions and in proportion of people having relapses compared with PBO group were maintained at 48 wks; early activity reflects removal of pro-inflammatory memory B cells -- by week 48, CD19+ B cells reconstituted to median of 30.7% of baseline, most of which were CD19+/CD27- naive B cells rather than CD19+/CD27+ memory B cells (Abstract #S12.003, AAN 2007; *New England Journal of Medicine* 2008 Feb 14;358(7):676-88; Abstract #S22.002, AAN 2008)

**Funding:** Genentech, Inc.

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00097188>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Rolipram (phosphodiesterase-4 inhibitor) **TERMINATED**  
**Purpose of study:** To control disease course and development of brain lesions  
**Possible mechanism:** Inhibits cAMP-specific phosphodiesterase, PDE IV  
**Study description:** Open label, crossover  
**Dose/route:** 3 mg tid po  
**Outcome parameters:** Gd lesions, frequency of relapse, scoring technique, MRI  
**Type of MS:** RR, SP  
**Number of Subjects:** 18  
**Start date:** January 2002  
**Observation period:** 14 months  
**Investigators:** R. Martin  
**Sites:** NIH, Bethesda, MD  
**Results/Publications:** Terminated after enrollment of 8 patients due to increase in average number of new (0.36 to 1.17) and total contrast-enhancing lesions (0.44 to 1.71) (Abstract #S22.001, AAN 2008)  
**Funding:** Intramural NINDS  
**ClinicalTrials.gov Link:** Not available  
**Last update:** 2008  
\*\*\*\*\*

**Agent:** RTL1000  
**Purpose of study:** To test safety  
**Possible mechanism:** Recombinant T-cell receptor ligands that bind to T cells, inducing a switch from inflammatory to anti-inflammatory  
**Study description:** Double blinded, placebo controlled, dose escalation  
**Dose/route:** In each cohort of 6 subjects, 4 subjects will receive a single dose of RTL1000 (2 mg, 6 mg, 20 mg, 60 mg, or 200 mg) iv and 2 will receive PBO iv  
**Outcome parameters:** EDSS, 25-foot walk, 9-hole peg test, MRI  
**Type of MS:** RR, SP  
**Number of Subjects:** 36  
**Start date:** January 2007  
**Observation period:** 3 months  
**Investigators:** V. Yadav and others  
**Sites:** MS Center of Oregon, Oregon Health & Science University, Portland, and others, United States  
**Results/Publications:** Not available  
**Funding:** Artielle ImmunoTherapeutics, Inc.  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00411723>  
**Last Update:** 2009  
\*\*\*\*\*

**Agent:** SB-683699  
**Purpose of study:** To investigate safety and effectiveness  
**Possible mechanism:** Reduces the number of active white blood cells entering the brain  
**Study description:** Randomized, double blinded, placebo controlled, parallel group, dose ranging  
**Dose/route:** po  
**Outcome parameters:** MRI at 6 months  
**Type of MS:** RR  
**Number of Subjects:** 350  
**Start date:** January 2007  
**Observation period:** 6 months  
**Investigators:** Multiple  
**Sites:** Multiple, Canada and Europe  
**Results/Publications:** Not available  
**Funding:** GlaxoSmithKline  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00395317>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Simvastatin + interferon beta-1a (Avonex<sup>®</sup>, Biogen Idec Inc.)  
**Purpose of study:** To determine safety and effectiveness in reducing disease activity  
**Possible mechanism:** Immunomodulatory  
**Study description:** Randomized, double blinded, placebo controlled, parallel  
**Dose/route:** Simvastatin 40 mg bid po + Avonex 30 mcg/wk im vs. PBO po + Avonex 30 mcg/wk im  
**Outcome parameters:** Frequency of relapse  
**Type of MS:** RR  
**Number of Subjects:** 380  
**Start date:** February 2006  
**Observation period:** Up to 24 months  
**Investigators:** P. Sorensen and others  
**Sites:** Multicenter, Denmark, Norway, Sweden, and Finland  
**Results/Publications:** Not available  
**Funding:** Biogen Idec  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00492765>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** Stress management program  
**Purpose of study:** To determine ability of stress management program to control MS inflammatory activity  
**Possible mechanism:** Improves glucocorticoid receptor function on immune cells  
**Study description:** Longitudinal, evaluator blinded  
**Dose/route:** Intensive cognitive behavioral stress management program (16 meetings with behavioral medicine specialist) vs. condensed cognitive behavioral stress management program (1-day workshop)  
**Outcome parameters:** Frequency of relapse, EDSS, MRI  
**Type of MS:** RR, SP  
**Number of Subjects:** 112  
**Start date:** March 2005  
**Observation period:** 12 months  
**Investigators:** D. Mohr  
**Sites:** University of California, San Francisco, CA; MS Center at Evergreen, Seattle, WA; Northwestern University, Chicago, IL  
**Results/Publications:** Not available  
**Funding:** NICHD  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00147446>  
**Last update:** 2008

\*\*\*\*\*

**Agent:** T cell vaccination (Tovaxin™, Opexa Therapeutics) **COMPLETED**  
**Purpose of study:** To delay conversion to clinically definite MS, or control disease course and development of brain lesions, also known as TERMS study  
**Possible mechanism:** Induces immunity against myelin-attacking T cells  
**Study description:** Randomized, double blinded, placebo controlled  
**Dose/route:** 5 injections of 30-45 million T cells sc at 0, 4, 8, 12, 24 wks  
**Outcome parameters:** MRI, frequency of relapse, EDSS, MSFC  
**Type of MS:** First clinical demyelinating event suggestive of MS, RR  
**Number of Subjects:** 150  
**Start date:** April 2006  
**Observation period:** 12 months  
**Investigators:** E. Fox and others  
**Sites:** Central Texas Neurology, Austin, and others, United States  
**Results/Publications:** Significant reduction in EDSS for Tovaxin group (28.1%) vs. PBO (5.6%); adjusted relapse rate reduced by 55% vs. PBO; Timed 25 foot Walk showed a benefit for Tovaxin over PBO; brain atrophy reduced by 88% and Gd lesions progressing to black holes by 20% in Tovaxin group; patients with less myelin T-cell reactivity had a lower risk of relapse; significant improvement in visual impairment scores on MSQLI; no serious adverse events (Abstract #P06.132, AAN 2009; Opexa Therapeutics press release, March 5, 2009)  
**Funding:** Opexa Therapeutics  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00245622>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** T cell receptor peptide vaccine (NeuroVax™, Orchestra Therapeutics)

**TERMINATED**

**Purpose of study:** To evaluate safety and effect on disease course

**Possible mechanism:** Stimulates regulatory (protective) T cells

**Study description:** Randomized, double blinded, placebo controlled

**Dose/route:** 300 mcg im every 4 wks for 44 wks vs. PBO

**Outcome parameters:** MRI

**Type of MS:** RR

**Number of Subjects:** 200

**Start date:** March 2007

**Observation period:** 48 weeks

**Investigators:** K. Selmaj and others, Europe

**Sites:** Multicenter, Europe

**Results/Publications:** Terminated study in August 2007 (Quarterly report, U.S. Securities and Exchange Commission)

**Funding:** Orchestra Therapeutics, Inc.

**ClinicalTrials.gov Link:** Not available

**Last update:** 2008

\*\*\*\*\*

**Agent:** Teriflunomide (HMR1726)

**Purpose of study:** To control lesion development, disease progression and relapses, also known as TEMSO study

**Possible mechanism:** Modulates responses of T-cells within the immune system by impairing DNA synthesis

**Study description:** Double blinded, placebo controlled

**Dose/route:** Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po

**Outcome parameters:** Frequency of relapse, EDSS, MRI

**Type of MS:** RR

**Number of Subjects:** 1050

**Start date:** Fall 2004

**Observation period:** 2 years

**Investigators:** P. O'Connor and others

**Sites:** St. Michael's Hospital, University of Toronto, and others, Worldwide

**Results/Publications:** Not available

**Funding:** sanofi-aventis

**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00134563>

**Last update:** 2008

\*\*\*\*\*

**Agent:** Teriflunomide (HMR1726)  
**Purpose of study:** To control lesion development, disease progression and relapses, also known as TOPIC study  
**Possible mechanism:** Modulates responses of T-cells within the immune system by impairing DNA synthesis  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po  
**Outcome parameters:** Conversion to clinically definite MS  
**Type of MS:** CIS  
**Number of Subjects:** 780  
**Start date:** February 2008  
**Observation period:** 2 years  
**Investigators:** A. Miller and others  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** sanofi-aventis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00622700>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Teriflunomide (HMR1726)  
**Purpose of study:** To control lesion development, disease progression and relapses, also known as TOWER study  
**Possible mechanism:** Modulates responses of T-cells within the immune system by impairing DNA synthesis  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** Teriflunomide 7 mg/d po vs. 14 mg/d po vs. PBO po  
**Outcome parameters:** EDSS, FIS  
**Type of MS:** RR  
**Number of Subjects:** 1110 (200 in the U.S.)  
**Start date:** September 2008  
**Observation period:** 3 years, 4 months  
**Investigators:** W. Byrnes and others  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** sanofi-aventis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00751881>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** Teriflunomide (HMR1726)  
**Purpose of study:** To control lesion development, disease progression and relapses, also known as PDY study  
**Possible mechanism:** Modulates responses of T-cells within the immune system by impairing DNA synthesis  
**Study description:** Randomized, double blinded, placebo controlled, parallel group  
**Dose/route:** Teriflunomide 7 mg/d po + Copaxone 20 mg/d sc vs. 14 mg/d po + Copaxone 20 mg/d sc vs. PBO po + Copaxone 20 mg/d scb  
**Outcome parameters:** MRI, EDSS, FIS  
**Type of MS:** RR, SP, PR  
**Number of Subjects:** 120  
**Start date:** May 2007  
**Observation period:** 64 weeks  
**Investigators:** Multiple  
**Sites:** Multicenter, worldwide  
**Results/Publications:** Not available  
**Funding:** sanofi-aventis  
**ClinicalTrials.gov Link:** <http://clinicaltrials.gov/ct2/show/NCT00475865>  
**Last Update:** 2009

\*\*\*\*\*

**Agent:** vitamin D3 **COMPLETED**  
**Purpose of study:** To determine safety  
**Possible mechanism:** Multiple immune mechanisms postulated (enhances macrophage phagocytosis, enhances activity of natural killer cells, inhibits production of Th1 cytokines, exhibits anti-tumor activity, inhibits transcription of IFN-gamma target genes)  
**Study description:** Controlled, non-blinded safety study  
**Dose/route:** 0 IU/d to 40,000 IU/d Calcium Phosphate 1200mg/d over 12 mos, then 0 IU/d to 40,000 IU/d over 6 mos vs. controls taking 0 and 4,000 IU/d  
**Outcome parameters:** Serum calcium, 25(OH)D, parathyroid hormone, alkaline phosphatase, urinary calcium/creatinine ratio, urinary N-telopeptide, cytokine profiles, matrix metalloproteinase protein-9, lymphocyte response assays, frequency of relapse, EDSS  
**Type of MS:** All types  
**Number of Subjects:** 50  
**Start date:** July 2006  
**Observation period:** 12 months  
**Investigators:** J. Burton, P. O'Connor  
**Sites:** St.Michael's Hospital, Toronto, Ontario, Canada  
**Results/Publications:** No calcium abnormalities; trend to clinical improvement; T-scores (a measure of T-cell reactivity to test antigens) dropped significantly over 52 weeks in treatment patients, but not in controls (Abstract # P20, World Congress of MS 2008; Abstract #P01.110, AAN 2009)  
**Funding:** Direct MS, MS Society of Canada  
**ClinicalTrials.gov Link:** Not available  
**Last Update:** 2009

\*\*\*\*\*

## Glossary

### ADVERSE REACTION

Also called Adverse Event. An unwanted effect caused by the administration of drugs. Onset could be sudden or develop over time. (See also Side Effects)

### APPROVED DRUGS

In the United States, the Food and Drug Administration (FDA) must approve a substance as a drug before it can be marketed and administered. The approval process involves several steps including pre-clinical laboratory and animal studies, clinical trials for safety and efficacy, filing of a New Drug Application by the manufacturer of the drug, FDA review of the application, and FDA approval or rejection of the application. (See also Food and Drug Administration)

### ARM

Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more. (See also Randomized Trial)

### BASELINE

The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment being tested. Safety and efficacy of a drug often are determined by monitoring changes from the baseline values.

### BIAS

When a point of view prevents impartial judgment on issues relating to the subject of that point of view. In clinical studies, bias is controlled by blinding and randomization. (See also Blind and Randomization)

### BLIND

A randomized trial is "Blind" if the participant is not told which arm of the trial they are on. A clinical trial is "Blind" if participants are unaware whether they are in the experimental or control arm of the study. Also called "masked." (See also Single Blind Study and Double Blind Study)

### CLINICAL

Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science.

### CLINICAL TRIAL

A clinical trial is a research study to answer specific questions about vaccines, new therapies, or new ways of using known treatments. Clinical trials (also called medical research and research studies) are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people.

Trials are in four phases (See also Phase I, II, III, and IV Trials):

Phase I tests a new drug or treatment in a small group.

Phase II expands the study to a larger group of people.

Phase III expands the study to an even larger group of people.

Phase IV takes place after the drug or treatment has been licensed and marketed.

#### COHORT

A group of individuals with some characteristics in common.

#### COMPASSIONATE USE

A method of providing experimental therapeutics prior to final FDA approval for use in humans. This procedure is used with very sick individuals who have no other treatment options. Often, case-by-case approval must be obtained from the FDA for "compassionate use" of a drug or therapy.

#### COMPLEMENTARY AND ALTERNATIVE THERAPY

Broad range of healing philosophies, approaches, and therapies that Western (conventional) medicine does not commonly use to promote wellbeing or treat health conditions. Examples include acupuncture and herbs.

#### COMPLETED

The study has concluded normally. Participants are no longer being examined or treated, i.e., last patient's last visit has occurred. (See also Recruitment Status)

#### CONTRAINDICATION

A specific circumstance when the use of certain treatments could be harmful.

#### CONTROL GROUP

The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo. (See also Placebo, Standard Treatment)

#### CONTROLLED TRIALS

Control is a standard against which experimental observations might be evaluated. In clinical trials, one group of participants is given an experimental drug, while another group (i.e., the control group) is given either a standard treatment for the disease or a placebo.

#### CHRONIC-PROGRESSIVE (CP) MS

Former "catch-all" term for progressive forms of MS, now categorized as two separate forms of disease. (See also Secondary-Progressive MS and Primary-Progressive MS)

#### CROSSOVER

A study design that has each patient in two or more treatments in a specified order.

#### DATA SAFETY AND MONITORING BOARD (DSMB)

An independent committee composed of community representatives and clinical research experts that reviews data while a clinical trial is in progress to ensure that participants are not

exposed to undue risk. A DSMB could recommend that a trial be stopped due to safety concerns or if the trial objectives have been achieved.

#### DOSE-RANGING STUDY

A clinical trial in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

#### DOUBLE-BLIND STUDY

A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, because the expectations of the doctor and the participant about the experimental drug do not affect the outcome. Also called double-masked study. (See also Blinded Study, Single-Blind Study, and Placebo)

#### DRUG-DRUG INTERACTION

A modification of the effect of a drug when administered with another drug. The effect could be an increase or a decrease in the action of either substance, or it could be an adverse effect that is not normally associated with either drug.

#### EFFICACY

Of a drug or treatment. The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the procedure mandated by the FDA, Phase II clinical trials gauge efficacy and Phase III trials confirm it. (See also Food and Drug Administration (FDA), Phase II and III Trials)

#### ELIGIBILITY CRITERIA

Summary criteria for participant selection. Includes Inclusion and Exclusion criteria. (See also Inclusion/Exclusion Criteria)

#### EMPIRICAL

Based on experimental data, not on a theory.

#### ENDPOINT

Overall outcomes that the protocol is designed to evaluate. Common endpoints are time to first relapse, toxicity, or disease progression. (See also Outcome Measure)

#### ENROLLING

The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process.

#### EPIDEMIOLOGY

The branch of medical science that deals with the study of incidence, distribution, and control of a disease in a population.

#### EXPERIMENTAL DRUG

A drug that is not FDA licensed for use in humans or as a treatment for a particular condition. (See also Off-Label Use)

#### FOOD AND DRUG ADMINISTRATION (FDA)

The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices.

#### HYPOTHESIS

A supposition or assumption advanced as a basis for reasoning or argument, or as a guide to experimental investigation.

#### INCLUSION/EXCLUSION CRITERIA

The medical or social standards determining whether a person might or might not be allowed to enter a clinical trial. Those criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

#### INFORMED CONSENT

The process of learning the key facts about a clinical trial before deciding whether or not to participate. It is also a continuing process throughout the study to provide information for participants. To help someone decide whether or not to participate, the doctors and nurses involved in the trial explain the details of the study.

#### INFORMED CONSENT DOCUMENT

A document that describes the rights of the study participants and includes details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits also are explained in the informed consent document. Based on the informed consent document, the individual decides whether or not to sign the form and participate in the study. Informed consent is not a contract, and the participant may withdraw from the trial at any time.

#### INSTITUTIONAL REVIEW BOARD (IRB)

A committee of physicians, statisticians, researchers, community advocates, and others who ensure that a clinical trial is ethical and that the rights of study participants are protected. All clinical trials in the United States must be approved by an IRB before they begin. Every institution that conducts or supports biomedical or behavioral research involving human participants must, by federal regulation, have an IRB that initially approves and periodically reviews the research to protect the rights of human participants.

#### INTENT TO TREAT

Analysis of clinical trial results that includes all data from participants in the groups to which they were randomized (See also Randomization) even if they never received the treatment.

#### INTERVENTIONS

Primary interventions being studied. Types of interventions are Drug, Gene Transfer, Vaccine, Behavior, Device, or Procedure.

#### INTRADERMAL (ID)

Introduced into the skin.

#### INTRAMUSCULAR (IM)

Injected into the muscle.

#### INTRAVENOUS (IV)

Injected into the vein.

#### INVESTIGATIONAL NEW DRUG

A new drug, antibiotic drug, or biological drug that is used in a clinical investigation. It also includes a biological product used *in vitro* for diagnostic purposes.

#### MRI

Magnetic resonance imaging. A non-invasive process of producing an image, especially of internal soft tissues of the body, from electromagnetic energy. MRI is used in MS to reveal lesions in the brain and spinal cord. It is used to confirm a diagnosis of MS and to track disease progression during clinical trials.

#### MULTICENTER STUDY

A clinical trial involving patients at more than one site open-label study—a study in which all patients receive the experimental treatment.

#### MULTIPLE SCLEROSIS, MAJOR FORMS

Although potential exists for the course of multiple sclerosis to progress from one pattern to a more severe one, the clinical course of MS usually falls within one of the following categories: relapsing-remitting, primary-progressive, progressive-relapsing, secondary-progressive.

#### NEW DRUG APPLICATION (NDA)

An application submitted by the manufacturer of a drug to the FDA—after clinical trials have been completed—for a license to market the drug for a specified indication.

#### OBJECTIVE

The reason for performing a trial in terms of the scientific questions to be answered by the data collected during the trial. The primary objective is the main question to be answered and drives any statistical planning for the trial (e.g., the sample size). Secondary and tertiary objectives are goals of a trial that will provide further information on the use of the treatment.

#### OFF-LABEL USE

A drug prescribed for conditions other than those approved by the FDA.

#### OPEN-LABEL TRIAL

A clinical trial in which doctors and participants know which drug/vaccine is administered.

#### ORAL

Taken by mouth.

## ORPHAN DRUGS

An FDA category that refers to medications used to treat diseases and conditions that occur rarely. There is little financial incentive for the pharmaceutical industry to develop medications for these diseases or conditions. Orphan drug status gives a manufacturer specific financial incentives to develop and provide such medications.

## OUTCOME MEASURE

Measurement unit used to assess the effectiveness of a program or intervention, such as measures of disease activity, progression, or changes in MRI scans. Read more about Clinical Study Measures used in MS trials.

## PEER REVIEW

Review of a clinical trial by experts chosen by the study sponsor. Those experts review the trials for scientific merit, participant safety, and ethical considerations.

## PHARMACOKINETICS

The processes (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

## PHASE I TRIALS

Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, to observe the side effects associated with increasing doses, and to gain early evidence of effectiveness. Could include healthy participants and/or patients.

## PHASE II TRIALS

Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.

## PHASE III TRIALS

Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained. Phase III trials are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling.

## PHASE IV TRIALS

Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

## PILOT STUDY

An early, small-to-moderate sized study, also known as a Phase 2 study. A pilot study follows the Phase 1 study, or "safety study," and is designed to begin determining the effectiveness of the experimental treatment.

## PLACEBO

A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments often are compared with placebos to assess the treatment's effectiveness. (See also Placebo Controlled Study)

### PLACEBO CONTROLLED STUDY

A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of participants, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see whether the investigational treatment is more effective in treating the condition.

### PLACEBO EFFECT

A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change could be beneficial, reflecting the expectations of the participant and often the expectations of the person giving the substance.

### PRECLINICAL

Refers to the testing of experimental drugs in the test tube or in animals—the testing that occurs before trials in humans may be carried out.

### PRIMARY-PROGRESSIVE (PP) MS

Form of MS characterized by disease progression from onset, with occasional plateaus (leveling of condition) and temporary minor improvements possible.

### PROGRESSIVE-RELAPSING (PR) MS

Form of MS characterized by progressive disease from onset, with acute relapses, with or without full recovery. Periods between relapses characterized by continuing progression. Considered to be a rare clinical course.

### PROTOCOL

A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial. The length of the study as well as the schedule of tests, procedures, medications, and dosages. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment. (See also Inclusion/Exclusion Criteria)

### QUALITY OF LIFE TRIALS

Also called Supportive Care trials. Refers to trials that explore ways to improve comfort and quality of life for individuals with a chronic illness.

### RANDOMIZATION

A method based on chance by which study participants are assigned to a treatment group. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant. (See also Arm)

## RANDOMIZED TRIAL

A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial. Occasionally placebos are utilized. (See also Arm and Placebo)

## RECRUITMENT STATUS

Indicates the current stage of a trial, whether it is planned, ongoing, or completed. Possible values include:

Not yet recruiting—Participants are not yet being recruited or enrolled.

Recruiting—Participants are currently being recruited and enrolled.

Enrolling by invitation—Participants are being (or will be) selected from a predetermined population.

Active, not recruiting—Study is ongoing (i.e., patients are being treated or examined), but enrollment has completed.

Completed—The study has concluded normally. Participants are no longer being examined or treated (i.e., last patient's last visit has occurred).

Suspended—Recruiting or enrolling participants has halted prematurely but potentially will resume.

Terminated—Recruiting or enrolling participants has halted prematurely and will not resume. Participants are no longer being examined or treated.

Withdrawn—Study halted prematurely, prior to enrollment of first participant.

## RELAPSE

A sudden worsening of preexisting symptoms, or the development of new neurologic symptoms, which lasts at least 24 hours. Synonymous with "exacerbation" or "acute attack."

## RELAPSING-PROGRESSIVE MS

Former name for progressive-relapsing MS.

## RELAPSING-REMITTING (RR) MS

Form of MS characterized by clearly defined disease relapses (flare-ups) with full recovery or with sequelae (resulting conditions) and residual deficit upon recovery. Periods between disease relapses characterized by a lack of disease progression (gradual worsening).

## RISK-BENEFIT RATIO

The risk to individual participants versus the potential benefits. The risk/benefit ratio could differ depending on the condition being treated.

## SECONDARY-PROGRESSIVE (SP) MS

Form of MS characterized by initial RR disease course followed by progression with or without occasional relapses, minor remissions (some recovery), and plateaus (leveling of condition).

## SINGLE-BLIND STUDY

A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking. Also called single-masked study. (See also Blind and Double-Blind Study).

#### STANDARD TREATMENT

A treatment currently in wide use and approved by the FDA, considered to be effective in the treatment of a specific disease or condition.

#### STATISTICAL SIGNIFICANCE

The probability that an event or difference occurred by chance alone. In clinical trials, the level of statistical significance depends on the number of participants studied and the observations made, as well as the magnitude of differences observed.

#### SUBCUTANEOUS (SC)

Injected under the skin.

#### SUSPENDED

Recruiting or enrolling participants has halted prematurely but potentially will resume. (See also Recruitment Status)

#### TERMINATED

Recruiting or enrolling participants has halted prematurely and will not resume. Participants are no longer being examined or treated. (See also Recruitment Status)

#### TOXICITY

An adverse effect produced by a drug that is detrimental to the participant's health. The level of toxicity associated with a drug will vary depending on the condition which the drug is used to treat.

#### TREATMENT IND

IND stands for Investigational New Drug application, which is part of the process to get approval from the FDA for marketing a new prescription drug in the United States. It makes promising new drugs available to desperately ill participants as early in the drug development process as possible. Treatment INDs are made available to participants before general marketing begins, typically during Phase III studies. To be considered for a treatment IND a participant cannot be eligible to be in the definitive clinical trial.

#### WITHDRAWN

Study halted prematurely, prior to enrollment of first participant. (See also Recruitment Status)

**This information is adapted from [ClinicalTrials.gov](https://clinicaltrials.gov), a service of the National Institutes of Health and developed by the National Library of Medicine.**